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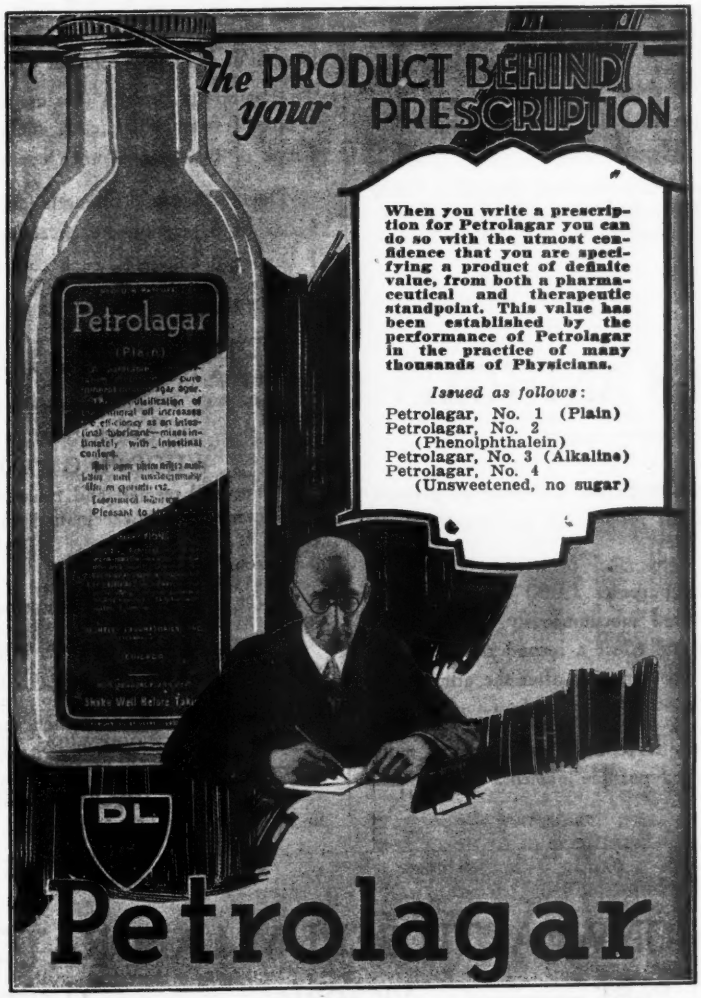
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COMBINED MEETING.—SECTIONS I. AND XII.

HYDATID ANAPHYLAXIS.

By H. R. DEW, F.R.C.S. (England),
From the Walter and Eliza Hall Institute, Melbourne.

(*Continued from page 320.*)

THE same phenomena have been recorded in cases of intraperitoneal rupture and there is no doubt that rupture into the large bile ducts may give similar severe symptoms. The following case history, for which I am indebted to Dr. Breidahl, of Stawell, exemplifies this.

Mr. A., *ætatis* fifty-three, had a hydatid cyst of his arm five years before; it was opened and after becoming infected, cleared up.

On February 13, 1925, he suddenly felt cold and had a rigor; his temperature rose to 38·8° C. with rapid faintness and failure of pulse.

In the early morning of February 14, 1925, he felt shivery again, a rash appeared in the form of discrete lumps all over the body. These were extremely irritable, but after a few hours disappeared and were followed by a diffuse erythema. The breathing at the same time became difficult, he became cyanosed, shivered, had a feeling of impending death and became pallid; his pulse rate was 130 and some retching occurred. Gradual improvement occurred.

On February 16, 1925, he had another attack with intense itching from the start; a dusky colour appeared; there was asthmatic breathing and he was almost pulseless; no heart sounds were heard with stethoscope and he appeared dead. Adrenalin (1‰) was given with good effect. This was repeated and he gradually improved.

On February 17, 1925, at operation a large hepatic cyst with bile-stained fluid and daughter cysts was evacuated.

In this case the previous cyst doubtless acted as a sensitizing agent. The recurrent attacks over a period of three days are interesting especially as they culminated in very severe anaphylactic shock. The appearance of the rash after twenty-four hours is also interesting and led in this case to the first suspicion of the nature of the disturbance. The leakage appeared to be into a bile duct as no evidence of an intravascular leak from this particular cyst was discovered at operation. A perusal of other similar cases forces one to the conclusion that absorption from the biliary tract can be rapid enough to cause anaphylaxis and there is no doubt that this phenomenon is the explanation of many unexplained symptoms in these and similar cases.

In these and in the grave cases it is important to note that urticaria is by no means constant so that it must not be taken as an obligatory criterion of hydatid anaphylaxis.

Benign Cases.

The benign cases form the largest group and I am sure if more accurate histories were obtainable and if the patient were closely questioned, these phenomena would be found in a much larger proportion of patients with hydatid disease than is generally believed. They are due to absorption of fluid in patients who are not highly sensitized. The commonest manifestations are cutaneous. Pruritus is common and often intense. Urticarial wheals which may occur in any part of the body or be localized in an inexplicable manner, are usual. Their appearance is often delayed for thirty-six to forty-eight hours after the actual rupture. McMurray[14] reported an interesting case of urticaria persisting over a period of two years which was cured at once after evacuation of an hepatic cyst. Erythematous rashes usually follow the urticaria and like it may be distributed in the region of the cyst or generalized over the whole body. They may persist for days or vanish as rapidly as they came. Dermatographism is sometimes present during the urticarial stage. These skin rashes are usually accompanied by other fugitive symptoms, such as momentary faintness, dyspnœa, vomiting and irregular fever. The last is common and may persist for some days. The true significance of these symptoms as anaphylactic phenomena has not often been recognized.

In an interesting case recorded by Verco[15] anaphylactic symptoms lasted over a period of two years. In this case urticaria and erythematous rashes with chronic induration of the skin occurred throughout this time, but after the evacuation of an hepatic cyst vanished in a few days.

Operative Interference and Anaphylaxis.

Owing to the abolition of the anaphylactic state by general anæsthesia grave symptoms rarely, if ever, occur at operation even if much hydatid fluid is spilt into the wound. There is no doubt that operations on these patients under local anæsthesia carry with them some risk of anaphylaxis and I have personally observed one patient operated upon by a colleague in whom a fatal result with all the symptoms of anaphylactic shock occurred.

However, in spite of general anæsthesia anaphylactic phenomena do occur after the effects of the anæsthetic have worn off and we are indebted to

Dévé[16] for emphasizing these interesting postoperative sequelæ. Most surgeons have been struck by peculiar postoperative symptoms even in uncomplicated hydatid cases, although few have recognized their true significance. These symptoms have been explained without any real confirmatory evidence as being due to reactionary pyrexia, operative shock, peritonitic reaction, postanæsthetic vomiting, mild infection of the area, absorption of blood or bile or slight secondary hæmorrhage. Unfortunately urticaria is usually absent and there is no absolute criterion by which we can distinguish the anaphylactic from ordinary postoperative shock with which they are of necessity inextricably mixed. In most cases respiratory symptoms are most common, taking the form of dyspnœa, cough and pyrexia, usually indicated in forty-eight hours.

Graver symptoms with dyspnœa, collapse and syncope out of all proportion to the operative trauma occasionally occur. In these transient urticaria or erythema is also noticed. These usually occur within twenty-four hours of operation. Dévé has drawn attention to a latent form which may not make its appearance for some days after operation. He has also distinguished a febrile form simulating pneumonia, an abdominal form in which pain, vomiting and extreme prostration may be found and a nervous form which is characterized by mental agitation, convulsions and even delirium.

Dévé records an interesting case in which postoperative death occurred.

Child, *ætatis* five years and a half, had a simple cyst of the liver which was punctured without any ill-effect, doubtless due to incomplete sensitization. Three weeks later under general anæsthesia operation of *formolage* and evacuation of the cyst was performed. No doubt some fluid was absorbed by the patient, for death occurred a few hours after the operation with all the symptoms of anaphylactic shock.

In this case it would seem that the preliminary puncture caused absorption of fluid and the lapse of three weeks was just sufficient to enable the anaphylactic state to be established. The interesting feature is that this occurred in spite of general anæsthesia. The graver cases are prone to occur in children and this has been emphasized by Dévé and Prudencio de Pena[12].

Another interesting phenomenon has recently been brought to my notice by a colleague.

The patient was a female, *ætatis* seven, and a simple hepatic cyst was evacuated and closed without drainage under general anæsthesia. For the four days after operation every suture puncture leaked blood continuously, so that for some time the case resembled one of hæmophilia. The oozing gradually ceased after the exhibition of serum and calcium lactate. In addition the patient's temperature ranged from 38·3° C. to 39·4° C. over a period of three weeks and she had occasional attacks of vomiting. At no time, however, was there any anxiety as to her ultimate recovery. It is possible that this condition may also be an anaphylactic manifestation.

An examination of the postoperative course of any series of patients reveals many cases of inexplicable pyrexia, dyspnœa, attacks of coughing or pain, which may be anaphylactic in origin.

Following on the operation and recovery the patient frequently remains sensitive for a long period and this is borne out by the result of the Casoni intradermal test in these cases (Dew, Kellaway and Williams[17]). Many of these patients give very brisk intradermal reactions and in some residual and recurrent cases repeated symptoms of an anaphylactic nature occur from time to time. These most frequently take the form of urticarial rashes or dyspnœic or pyrexial attacks. In one patient who had a persistent sinus leading down to hydatid disease of the vertebræ, periodical discharge of collapsed daughter cysts occurred. This patient could always tell when a cyst or series of cysts had ruptured by the occurrence of a sensation of lassitude, irregular fever, cough, erythema in the area of the wound and urticarial wheals in various parts of the body. These symptoms appeared before the discharge and were obviously due to absorption of fluid from the ruptured cysts.

Another patient who had an hepato-bronchial communication and who for some months after operation expectorated collapsed bile-stained daughter cysts, was able by his symptoms to predict the expectoration of collapsed cysts. In this case asthmatic symptoms, cyanosis, headache and urticaria were associated with rupture of daughter cysts. The urticaria appeared on the arms only and was intensely itchy. This patient ceased expectorating hydatid membrane a few months after the operation and since that time all these symptoms have disappeared.

These postoperative cases show that resensitization tends to occur after rupture and that apparently anaphylactic symptoms can be repeated almost indefinitely.

In summation the following facts must be emphasized:

1. Exploratory puncture of even a simple cyst is dangerous and may even be fatal; in this eventuality anaphylactic shock is often the main factor.

2. The degree of sensitization of patients with hydatid disease varies. It is certainly higher in patients who have undergone some complication such as rupture, operative interference, puncture or recent suppuration. In these cases any operative interference after a period of fourteen to twenty-one days or even earlier may be followed by some anaphylactic symptoms.

3. Operation under local anæsthesia is not without risk of anaphylaxis, especially in complicated cases.

4. General anæsthesia greatly reduces anaphylactic sensitiveness, but owing to the spilling of fluid at operation delayed symptoms may occur after operation. For this reason careful technique is essential, in the way of packing, removal of fluid quickly and so forth.

5. The mode of reaction to the Casoni test may be a useful preoperative guide. If the second or erythematous stage of the reaction is present, especially if very evident, there is danger of anaphylactic symptoms following absorption of fluid. If a wheal only is produced or the second stage is a mild reaction, the risk will be slight.

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THE MEDICAL ASPECT OF HYDATID DISEASE.

By R. R. STAWELL, M.D. (Melbourne), D.P.H. (London),
Honorary Consulting Physician, Melbourne Hospital; Honorary Consulting Physician, Children's Hospital, Melbourne.

I HAVE the honour to present to you the subject of hydatid disease, considered from the point of view of the practising physician. Though this is an old subject, recently a great deal of new work has been done on it by Dr. Dew, Dr. Kellaway, Dr. Fairley and Miss Williams, of the Walter and Eliza Hall Institute of Medical Research in Melbourne; part of that new work I would propose to indicate to you. Now, seeing that there is no medicinal remedy for this disease, the subject resolves itself for us into (i) the recognition of the disease in the human host, (ii) the prevention of its occurrence there.

First then let me consider the clinical diagnosis. In the chain of evidence indicating the presence of hydatid disease, there are five or six links which must be pieced together for a satisfactory diagnosis. These links are:

1. The toxic symptoms, largely unrecognized, until recently, as of special significance.
2. The physical signs, including the results of X ray examination.
3. The special complement fixation test.
4. The Casoni reaction, as recently interpreted by the Melbourne workers.
5. The occasional presence of eosinophilia in the blood.

All these are links as it were of circumstantial evidence.

6. There is, of course, the occasional presence of hydatid hooklets and of actual cysts in the sputum and the excreta, which when found by an expert is proof of the presence of the disease.

Now the so-called toxic symptoms must be recognized as manifestations of anaphylaxis, that is of an abnormal degree of sensitiveness to irregularly recurring absorption of varying amounts of hydatid poison, a hypersensitiveness induced in the first instance at the time of the original infestation of the human host by the hexacanth embryo of the ova of the *Tænia echinococcus* of the dog.

This infestation occurs most commonly in childhood, as has been clearly shown by the investigations of Dew and others.

Absorption of hydatid poison occurs whenever the hydatid cyst is injured, even when the injury has been very slight. Such injurious influences are (i) any mechanical traumatism which leads to actual rupture of the cyst wall, or which is just sufficient to injure the cyst wall without obvious rupture, and (ii) biochemical substances, such as bile or mild bacterial infection, which impair the viability of the cyst.

If the degree of injury is severe enough to produce instant and complete rupture of the cyst, the toxic manifestations are fulminating and may be fatal.

Among the toxic symptoms the most commonly recognized are those that affect the skin, such as urticaria, erythema and pruritus; these may all be very mild and transitory and when they do occur in that mild form are most frequently misinterpreted. This error in interpretation is likely to occur when these cutaneous signs are associated with anaphylactic gastro-intestinal symptoms, such as abdominal pain, vomiting and diarrhœa and especially when these are further associated with a general constitutional disturbance, as shown by an irregular pyrexia and anaphylactic symptoms affecting the nervous systems, such as restlessness, and in childhood possibly convulsions.

The common diagnosis of such a syndrome of symptoms in adults is ptomaine poisoning and in children worms; how near to and yet how far from right is the latter diagnosis.

A further incidence of anaphylactic response is upon the respiratory system, producing an asthma-like cough, dyspnœa and even cyanosis, and still worse are the cardio-vascular disorders, leading to syncope, shock and even death.

I may point out in passing that none of these symptoms, inseparable sequelæ as they are to the escape of hydatid fluid, occur at the time of a surgical operation on a hydatid cyst, because general anæsthesia abolishes the anaphylactic state, although as Dévé has pointed out, this state may supervene as a postoperation phenomenon.

Apart from grave and mild anaphylactic symptoms, there occasionally occurs a chronic condition of ill-health, called the "hydatid diathesis," probably this is genuinely toxic in basis. I have seen this condition in cases of multiple omental hydatids associated, of course, with an original hydatid cyst of the liver.

And now to pass on to the consideration of physical signs of hydatid disease of the liver and of the lungs, for to this disease of these organs I shall

restrict my remarks; for the sake of brevity, these remarks must be made to appear, I am afraid, as unnecessarily aphoristic in tone.

Firstly, all enlargements of the liver in persons of all ages, in all sheep-breeding countries, must be suspect of hydatid.

Secondly, all cases of jaundice with hepatic enlargement and with or without attacks of pain, must be particularly investigated to exclude hydatid. The commonest error is to diagnose the presence of gall stones and to overlook the presence of a hydatid cyst. Jaundice is not a specially common symptom in uncomplicated cholelithiasis or cholecystitis, while it is a very common sign associated with an infected or a ruptured hydatid cyst of the liver.

Thirdly, obscure cases of cirrhosis of the liver, whether small or large and with or without jaundice, must be considered as possibly and in children, probably associated with the presence of an hepatic hydatid. In persons past middle age the hydatid cyst may have retrogressed, producing in the process, spoiling of liver cells.

Fourthly, all abnormal hepatic physical signs must be linked up, after inquiry, with the possible occurrence in the past of the toxic symptoms to which I have referred.

Recurring urticaria or persisting pruritus must not just be accepted as due to the presence of jaundice; irregular pyrexia must not be accepted as due only to a hypothetically persisting cholecystitis.

Fifthly, an X ray examination of the contour of the convex surface of the liver should always be made.

Sixthly, in spite of textbook statements, the hydatid thrill is rarely found as a physical sign and may be ignored.

To pass on to a consideration of the physical signs of hydatid disease of the lungs, it can be said at once that the X ray examination far transcends in practical importance all other methods of physical examination; but there are pitfalls for us even here. For instance a ruptured hydatid cyst of the lung may give very indefinitely-shaped shadows and radiologically cannot be distinguished from an abscess of lung or an irregularly-shaped, saccular, bronchiectatic cavity. Again, a pleurisy with a large effusion may obscure the radiological signs of an underlying hydatid cyst. And further I must point out that the presence of the tubercle bacilli in the sputum does not exclude the concurrent presence of a ruptured or unruptured hydatid cyst in the same lung. Not to look for a cyst under these circumstances may be pardonable. It is an error I once made myself; it was a lesson to me.

Now, it comes to this, having suspected by circumstantial evidence indefinite symptoms and not very definite signs, the presence of hydatid disease; how can we prove it? In these days, we can go a long way to proving it by the laboratory method of specific complement fixation and by the special Casoni reaction as recently interpreted by the Melbourne workers. Without these tests it is more than likely that not far off a 50% error will be made in the actual diagnosis of hydatid disease up and down the body and in deep-seated organs; the error, of course, will be actually much less in the clinical diagnosis of hydatid disease of liver and lungs.

I feel it is not for me to consider with you any of the many points of interest that are associated with the clinical application of the complement fixation test and the Casoni reaction, for the subject of hydatid tests of clinical interest will be dealt with by Dr. Kellaway, a well recognized authority on the subject; but I may say that by the combination of alert clinical examination and these tests, the error of diagnosis in hydatid disease has been reduced in the Melbourne Hospital from about 40% to about 2%. The value of these tests far exceeds the value of the occasional occurrence of eosinophilia in the blood.

In conclusion I must say a few words about the preventive medicine aspect of hydatid disease; again I shall have to make statements expressed in dogmatic form.

1. Hydatid disease starts commonly as a disease in childhood; infestation occurs during that vulnerable age. The children are infected directly from dogs, not indirectly from water or from food.
2. The incidence of the disease in childhood in any special district could be proved by the Casoni test.
3. The dogs are infested from eating the raw offal, the lights and liver of infected sheep.
4. The plan, the only plan of ultimate prevention is to prohibit the feeding of dogs with hydatid-infected raw material.

THE X RAY EXAMINATION OF INTRATHORACIC AND SUBDIAPHRAGMATIC HYDATID DISEASE AND ITS COMPLICATIONS.

By NEIL GUTHRIE, M.C., M.B., Ch.B., D.M.R.E. (Cambridge),
Radiologist, Christchurch Hospital,

THIS paper is based upon the comparatively short period of five years' radiological experience in a community where hydatid disease is prevalent. It is not written with the intention of advocating an X ray examination in preference to any of the other means by which we may detect the echinococcus in man. With this disease which may make a settlement in any vascularized tissue of the body, there is no single method that can be universally relied upon for its detection and localization.

In presenting some of the aspects of the X ray appearances I cannot too strongly emphasize the necessity for a combination of all our resources in diagnosis and a mutual assistance between those who are concerned in conducting the examinations.

The detection of an uncomplicated hydatid cyst by means of X rays depends upon the nature of the tissue in which it is embedded. If the pericystic medium has either increased or decreased radiability compared with that of the hydatid, the cyst will be defined by the resulting contrast on the screen or film. The two situations in which such contrast is

obtained *par excellence,* are in bone and in the thorax.

In bone the X ray examination will demonstrate cavitation. However, even when the echinococcus is considered as a possible cause, the differential diagnosis may be difficult from other diseases which produce a cystic appearance, though all the resources of medical investigation are brought to bear on the case.

It is customary to find it stated in textbooks that cysts in the lung offer no difficulty in diagnosis. They are described as casting an ovoid or circular shadow of homogeneous intensity with an even well defined outline. This textbook conception of the disease is misleading. The typical cystic appearance is frequently very much altered either by its surroundings or by complications which have occurred before the patient seeks medical advice.

Uncomplicated cysts may be totally masked by the heart or only the lateral margin of the shadow may be visible in the neighbourhood of the costo-phrenic angle. As viewed anteriorly or posteriorly on the screen or in a radiogram exposed for pulmonary diagnosis, the appearances may closely resemble a small hydrothorax or pleural hyperplasia obliterating the lower and outer portion of the lung field. Sometimes the periphery of the cyst will present an even, fairly well defined curve which has the opposite direction to that seen when a moderate quantity of fluid is present in the pleural cavity. Skiagrams should be taken, with the Potter-Bucky diaphragm, in the dorsal or ventral position and in the left lateral position with exposures similar to those used in renal diagnosis. From my experience I would strongly emphasize the value of this technique.

When one is confronted with a shadow lying clearly in either lung field, having the classical characteristics of a hydatid cyst, it is well to remember other conditions which may present a similar appearance. I made an erroneous diagnosis in one such case. The tumour shadow with a circular outline and a homogeneous density was localized close to the posterior parietes in the upper portion of the right hemithorax. At operation the surgeon could not find a cyst. In endeavouring to localize it by aspiration the syringe was filled with blood. Necropsy showed a globular sarcomatous growth originating from the posterior portion of a rib and projecting towards the pleural cavity. When the film was reviewed with the knowledge of the *post mortem* findings, a portion of the rib outline about 2·5 centimetres long was seen to be lost. There was evidence in the film on which to base a correct diagnosis, but it was not observed in the first instance.

Heuser[1] states that primary sarcoma of the lung may present appearances which are indistinguishable from those of a cyst.

Secondary metastasis of the embolic type may resemble hydatid, but in these cases the primary tumour will usually have been detected elsewhere.

A very large cyst occupying the major portion of one hemithorax may closely resemble a large pleural effusion. In my experience an examination conducted in the erect position will on full inspiration reveal the lower border of the cyst or give an illumination of the costo-phrenic angle which is not seen in a large hydrothorax. In the largest cyst which I have seen there was no displacement of the heart or mediastinum.

Hitherto I have been dealing with the disease in the thorax in its simple cystic stage. Some of the complications which might occur and which will alter the classical appearances, will now be considered.

Frequently as the result of complicating occurrences an investigation into the history combined with the objective signs and biological examinations will give an indication of the primary cause of the patient's illness. But the X ray examination is not simplified by this knowledge. One is confronted with the interpretation into terms of pathology of the compounded shadows made up of a more or less mutilated cyst, the superadded disease of the lung and pleura and displacements of intrathoracic structures.

Spontaneous rupture into the pleural cavity. One such case has been encountered. The physician had made a correct presumptive diagnosis as proved by operation. The X ray appearances were those of a large hydrothorax with displacement of the heart and mediastinum, but without any evidence indicative of hydatid disease.

I have seen cases in which spontaneous rupture had occurred into a bronchus and in all instances I was informed that portions of membrane had been detected in the sputum. In one case the history indicated that rupture had occurred five years previously by the expectoration of nearly a pint of clear salty fluid. There was an opacity of the lower two-thirds of the right lung field due to pleural thickening and pulmonary consolidation. No cyst could be defined. Fibrosis with traction of the trachea was present in the region of the upper limit of the opacity. At operation organization between the parietal and visceral pleura was found and the cyst was localized in consolidated lung. In another case the partly collapsed cyst was demonstrated bordering on the heart shadow and lying between it and the axillary parietes with the left diaphragm raised in position and fixed by adhesions. Cicatrization from healing of a cyst previously operated upon was present at the apex causing traction displacement of the trachea.

I have examined a patient in whom rupture from needling had occurred into the pleural cavity. There is one warning that should again be emphatically sounded in cases of intrathoracic hydatid; that is the grave danger of needling for diagnostic purposes. An X ray examination should take precedence of this procedure as it is free from danger to the patient.

No patients have been seen in whom suppuration has occurred in an unruptured intrathoracic cyst. Should infection take place in an unruptured cyst, it is inferred that its contour would be masked by peripulmonitis or fluid in the pleural cavity.

Heuser[1] has pointed out that cysts are sometimes masked by an accompanying hydrothorax.

By ordinary means an X ray examination of abdominal hydatids will frequently be of little or no assistance except when the disease is located on the upper surface of the liver or spleen.

In these cases the fluoroscope and the radiogram will afford valuable information and sometimes give evidence upon which a positive diagnosis of cyst may be based. The whole arc of the diaphragm on one side may be displaced upwards or there may be only a localized bulging of a segment. Respiratory excursion is usually unimpaired when the phrenic contour has a clear cut outline. When respiratory movement is restricted or absent, there is often evidence of pleural thickening, information which will be appreciated by the surgeon. Not infrequently, however, one is unable from the X ray examination to differentiate hydatid disease from other conditions which may give rise to an upward projection of the diaphragm. In such cases the correct diagnosis is likely to be revealed only by a correlation of the clinical aspect of the case with the biological and radiological findings. But there is one method of X ray examination in this differential diagnosis which is invaluable. A good quality radiogram should be obtained in the lateral position with the film lying against the affected side. By this means I have been able on occasions to demonstrate a cyst which was not discernible in films exposed in the anterior or posterior position.

Should infection have occurred or should a cyst have ruptured through the diaphragm, all evidence of the primary disease may be obliterated. Furthermore, it may be impossible in these cases to state whether the pleuro-pneumonic infection originated in the thorax or whether it was due to extension from below the diaphragm.

Where the ordinary X ray examination is likely to fail in abdominal hydatids, pneumo-peritoneum is likely to succeed except when the cyst is situated in a solid organ or is of small size on the under surface of the liver. Though I have advocated this procedure in some cases I have not yet had the opportunity of using it.

Occasionally one meets with cysts in which calcification has taken place and in these cases there is little difficulty in demonstrating the structural change, no matter where it happens to be situated. One is, however, still faced with the differential diagnosis from calcifications which may present a similar appearance.

As has been pointed out by Anderson[2] displacements and defects may be shown in the barium filled stomach or intestine. A case[3] has been recorded of a pressure filling deformity of the gall bladder which was examined by the method introduced by Graham.

I have dealt only with the initial diagnosis, but the radiological examination is of great value to the surgeon, particularly in intrathoracic cases, in illuminating post operative complications, such as incomplete drainage, hydro-pneumothorax, recession of the lung, lung abscess and hydrothorax.

Lastly, follow up examinations, show the progress of recovery and in conjunction with the subjective and objective signs, assist in determining the degree of restoration to health.

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DR. L. E. BARNETT (Dunedin) stated that hydatid disease was readily understood provided that one knew the life history of the *Tænia echinococcus* by reference to a diagram of the surrounding adventitia and the two membranes of a cyst (ectocyst and endocyst). He explained that if the cuticle or endocyst were intact, no absorption of hydatid fluid took place, but if owing to its friability it were ruptured, as it might easily be, even by a blow or by violent muscular exercise, some of the contents escaped and anaphylactic symptoms resulted. Often bile from unobliterated bile ducts entered and being mildly septic made suppuration possible.

DR. S. V. SEWELL (Melbourne) referred to the histories of two patients whose sputum had contained tubercle bacilli; in addition, there was a hydatid cyst which might easily have been overlooked. In one instance surgical treatment of the hydatid led to improvement of the tuberculosis. In the other an exploratory puncture revealed pleuritic fluid, but in addition ruptured a hydatid cyst, with nearly fatal results from severe anaphylaxis.

He further spoke of the condition of a patient in whom sudden pulmonary symptoms after appendicectomy caused pulmonary embolism to be suspected, but from erythematous patches and left-sided pneumothorax hydatid disease was diagnosed; death from anaphylaxis had narrowly been averted by adrenalin.

In another patient diarrhœa and vomiting had been accompanied by urticaria; hydatid cyst had been diagnosed and found in spite of the fact that there was no reaction to the Casoni test; the hydatid complement fixation was obtained.

DR. S. S. ARGYLE (Melbourne) stated that in his experience sarcoma might be mistaken for hydatid cyst on radioscopic evidence; pleurisy with effusion did not exclude the possibility of a hydatid cyst which might produce a shadow in the skiagram after the removal of the fluid.

DR. R. R. STAWELL (Melbourne) expressed his appreciation of Dr. Barnett's contribution and agreed that any mild, unrecognized traumatism could produce some liberation of hydatid fluid. All those things called toxic were of an anaphylactic nature. He referred to the so-called hydatid diathesis; the patient was not hypersensitive to and did not react to the hydatid fluid, but was gradually poisoned by it. He knew of two patients who had had multiple omental hydatids and had gone slowly down under this gradual poisoning.

He referred to the problem of surgical technique, the abuse of which meant the resowing of the disease.

In his opinion mild degrees of anaphylaxis should be searched for as a routine in children of all ages. In Australia in his experience hydatid disease was lessening.

He referred to the public health museum where the wrong methods of avoidance were being illustrated. The avoidance of drinking unboiled water and of keeping dogs about the house was propaganda of twenty years ago. The hydatid ova when excreted were heavier than water and sank into the mud. Moreover, the ova were very vulnerable to air and sunlight and their viability outside the host was very slight. Dogs should be prevented from

eating raw liver and lights and offal of sheep. If these were boiled, the incidence of hydatids would be reduced to a minimum.

The Casoni test applied to school children would be a reasonable method of determining the incidence of the disease. He admitted that he knew of many instances in which the infection had not occurred in childhood, but was due to massive infections during adult life.

DR. R. N. GUTHRIE (Christchurch) suggested periodically breaking the cycle in dogs by administering anthelmintics every six months.

Dr. Stawell objected that the dogs would be readily reinfected.

DR. L. E. BARNETT (Dunedin) agreed that they should give up teaching that water was a frequent source of hydatid infection. Though he used to teach the vegetable and water theory of infection, he had already called the attention of the authorities to the fact that it had become out of date and that hydatid infection occurred from direct contact with dogs. It was one of the maladies of dirty hands. Many years ago hydatid disease was very prevalent in Iceland. Women had been more commonly affected than men. The explanation lay in the fact that hydatid ova were caught in the wool of sheep. It was the women who used to milk the sheep and therefore got hydatid ova on their hands. When they gave up the milking of sheep, this disproportion disappeared.

ARTIFICIAL PNEUMOTHORAX WITH AND WITHOUT "LIPIODOL" IN DIAGNOSIS AND TREATMENT OF LUNG CONDITIONS.

By J. F. MACKEDDIE, M.D.,
Physician Attending In-Patients, the Alfred Hospital, Melbourne.

"Too little is known of artificial pneumothorax in this country," said Dr. Burrell, of Brompton Hospital, in his report to the Medical Research Council in 1922. In spite of much enlightenment on the subject, the same might still be said of England. It is over forty years since Forlanini practised artificial pneumothorax in Italy and it was not till twenty-five years later that England became acquainted with it. In 1909 Dr. Lillingston, himself a tuberculous patient, returned from the Mesnalian Sanatorium in Norway with air in his chest and began to make known and to practise the treatment that had saved him. Needless to say Australia is open to the same indictment as England. It is at first a little difficult to assign the reason of this backwardness. The beneficial results of artificial pneumothorax in tuberculosis of the lung have been so striking that its universal use would have been easily predicted. What then has been the retarding influence?

We may place easily first the fact that the early leaders in this movement were divided in opinion as to the class of case most suitable for it. Clive Rivière, one of the earliest workers in this field in London, was and is still very conservative. He would not use artificial pneumothorax for early tuberculosis in a patient who had a reasonable chance to recover by the more conventional methods. Morriston Davies hails every early unilateral tuberculous infection as the ideal one for artificial pneumothorax. All of course were agreed on the advisability of artificial pneumothorax in more or less advanced unilateral cases (even with considerable involvement of the other side) as a last resort.

Again, it is not easy to decide to what extent the good side may be involved and yet respond hopefully to the collapse of the bad lung. This indefiniteness does not conduce to enthusiastic acceptance of a new method of treatment. Further, there has been some diversity of opinion about the best way of entering the pleural cavity. A particular kind of needle in the hands of an expert may not do what is asked of it by the beginner. The undoubted occurrence of disaster to the expert himself is very disquieting, all the more because the nature of what is called "pleural shock" is unknown, as are also the means of its prevention.

Lastly, an artificial pneumothorax is the beginning of a series of refills that demands perseverance both on the doctor's and the patient's part and has to be accompanied by frequent collateral X ray work.

Probably if it were conceded all round that a patient with undoubted early unilateral tuberculosis should be subjected to artificial pneumothorax at once, less harm would result than has followed from the wholesale neglect of this therapeutic agent.

Woodcock in 1915 said: "There are dangers attendant on artificial pneumothorax, but the greatest—and about this let there be no mistake—is the neglect in which it is held."

Again, for beginners one type of needle should be insisted on as less likely to be followed by failure.

Emphasis should be laid on the fact that some (in some cases, considerable) involvement of the good side does not negative artificial pneumothorax. As for pleural shock, the only thing to do is to feel confident that it is not going to happen to you. It does not seem to have any relation to the preparation of the patient, as to whether morphine has or has not been given; nor does it occur exclusively in initial fills.

X ray help should be unsparingly drawn on. Do not trust to probabilities and lastly from our experience at the Alfred Hospital, I would advise *post mortem* practice. You learn two things in no other way; the surprisingly short distance there is from skin to parietal pleura and the feel of the needle against the pleura.

The Apparatus.

Forlanini's apparatus is still in use, but has been largely replaced by a simpler type, Lillingston's. A few minutes' manipulation makes one quite familiar with it.

In Figure I *A* and *B* are plain bottles of one litre capacity; *A* being the bottle that delivers the air, is graduated. Through a tightly fitting rubber cork a glass tube *D* is passed down to the bottom of *B*; bent at the top it is connected by rubber tubing to a similar tube let down into *A*. If *B* is filled with a liquid which we wish to transfer to *A*, we start a siphon action by blowing down the short glass tube *F*.

Suppose we stop the flow *A*-wards by clamping at *S* when the level is at zero in *A*. If we fit a short

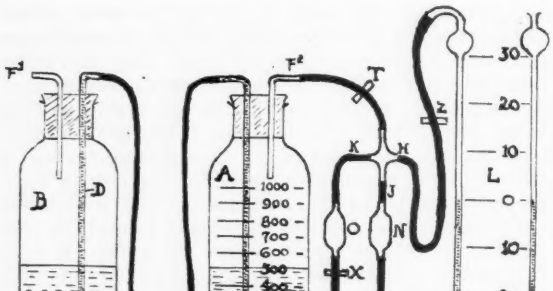

FIGURE I.

glass tube F^2 into A, we convert the latter into a delivery bottle. By unclamping at S we allow the liquid in A to rise and drive out air at F^2. How do we acquire this air? By reversing the process. Thus, $+F^2$ is attached to a four-way glass piece; H connects one of the ways to one limb of a manometer L; tubing K connects another way with the external air; tubing J goes to the delivery needle. If we shut off at Y and at Z and leave T, S and X open and then lower B, we shall deplete A of liquid and fill it with air drawn through F^2 from K which leads from air. O and N are glass connecting bulbs packed with cotton wool, so that the air is filtered on receipt and on delivery. The needle is not fitted directly on to P, three or four centimetres of glass tube intervene, so that if the needle pierce a vessel, blood soon shows at O. The liquid in the bottles is 1% carbolic acid solution with a little colouring matter. The same may be used in the manometer tubes. When not in use small glass rods are fitted into the ends of tubing K and J. Tubing is boiled frequently and the glass bulbs freshly charged with wool. Before use, the connexions must be tested. A negative or a positive pressure is made in the manometer; the tubes are then clamped off and you see if any air escapes. When the needle is being passed into the chest, S, X and T are all clamped off, leaving the delivery needle connected up with the manometer only by unclamping at Y, Z.

Needles.

Clive Rivière's needle has the most adherents. It is really a trocar and cannula. The trocar projects beyond the end of the cannula far enough to make it serviceable and sometimes the cannula mouth is sharpened to make it bore through the pleura more easily. Once the pleura is reached, the trocar is withdrawn and the pleura entered by the cannula, the tap of the cannula being turned off at the same time. A favourite way, too, is to take the point off a fairly large needle with a file, to make a puncture in the skin with a scalpel and push the blunt needle on to the pleura. There will be no mistaking the pleura with a blunt needle and this is pushed into the cavity without injuring the lung.

A method I have found very satisfactory at the Alfred Hospital is to fit a needle with a stout blunt stilette that projects a fraction beyond the needle point. The needle enters the chest wall with the stilette drawn into the needle. Once under the skin the stilette is pushed well home and the pleura encountered by its blunt end, which can readily be pushed through the pleura. On its withdrawal the needle will be left in the pleural cavity, the tap being turned off as the stilette is withdrawn.

Preparation of Patient.

Burrell in the initial fills always gives calomel the preceding night and magnesium sulphate in the morning; the actual artificial pneumothorax is preceded half an hour by fifteen milligrammes of morphine or one cubic centimetre of a 2% solution of "Omnopon." Others omit the morphine. We do not as a rule give any at the Alfred Hospital. Other things besides a purgation and sedative enter into the preparation of the patient. Every patient comes to artificial pneumothorax with great trepidation and it is of first importance that we get his confidence, explaining what we are going to do to his lung, even, perhaps, showing him a plate of a lung so treated. The presence in the ward of another patient who has been successfully through the initial stage and who has discovered that "there was nothing in it" is a great stand-by. Anyway, you can promise the patient that you are not going to give him a bad time and with good anæsthetizing and a little pains you can keep your promise and you have henceforth a willing patient.

Our habit at the Alfred Hospital is not to let the patient know, much less see by the manometer what is actually taking place. Thus, if we fail, he is none the wiser and is not disappointed. Needless to say, if it be the operator's first case, the trepidation is not all on the side of the patient and the possibility of an uncomfortable quarter of an hour has always to be faced.

The Operation.

You are generally told to anæsthetize the skin over a rib and then to pull the anæsthetized button of skin down to the interspace below. The beginner had better anæsthetize over the interspace which he intends to enter. It is of great importance that when you get your needle into the pleural cavity, you hold it firmly there. If you have drawn down the skin, it may fly up again at some stage and flick your needle out of the pleural cavity. Having anæsthetized intradermally a small button of skin, you pass the needle down vertically, delivering the anæsthetic as you go, pausing at short intervals to allow the anæsthetic to prepare your way for further pushes. Push the fluid well into the pleura.

The site of election is the fourth or fifth interspace in the mid-axilla. Failing entrance here, a corresponding spot in the back is tried. Burrell's habit is to have two such tries and no more. In a day or two he will try perhaps lower down in the axilla or somewhere in the posterior line of the

axilla or at the base of the lung posteriorly. He repeats the trial twice only and then abandons the case as unsuitable for artificial pneumothorax and all this without giving the patient pain or even discomfort.

The apparatus is set up with the fluid at the same level in both bottles. The needle is dried in a spirit flame and attached to the delivery tube. It is wise to pass one hundred cubic centimetres through the tube before use. The needle is then pushed into the chest, connected only with the manometer. You feel your way into the pleura, withdraw stilette or trocar, turning off the tap on the needle at the same time and if the needle is in the pleural cavity the fluid in the manometer will give good movements. In the negative limb *L* it will move up on inspiration and down on expiration. There will be no doubt about the movements. Then clamps *S* and *X* are loosened and though the fluids are at the same level, the negative pressure in the thorax will draw in fifty or one hundred cubic centimetres. *B* can then be raised somewhat so as to accelerate the delivery. Dr. Burrell is usually content with, say, 250 cubic centimetres unless, of course, the reason for the compression was hæmoptysis, when he aims at a complete compression. He is content to convert the initial negative pressure of, say, −12−4 to −8−2.

In recording pressure the figure is doubled. If the fluid rises to −6 in *L* on inspiration, we record −12 and if it falls at expiration to −2, we read −4.

The above is the record of an uninterruptedly successful artificial pneumothorax. You may be sure soon to strike divergences from the above which will be perplexing.

Difficulties.

You think that the needle is in the pleural cavity, but the very small oscillations of the manometer make you hesitate. Probably the needle is against the parietal pleura and not through it.

If the needle is in a cavity or bronchial tube, there will be oscillations up and down in the neighbourhood of zero, larger than in the last condition. One litre of air could easily be passed into a bronchial tube without altering the manometer. Dr. Burrell has penetrated a bronchial tube with the needle and being in doubt as to where it was, has put a little pepperminted cotton wool on the end of the needle, then turned on the tap of the needle and the patient has tasted the peppermint.

The manometer shows a good negative pressure with some oscillation, but the oscillations cease while the negative pressure increases on each inspiration. The probability is that the needle is in the pleural cavity, but the visceral pleura is fouling the needle. A little air allowed in gently will soon reestablish oscillation. If there are no oscillations, the needle is not in the pleural cavity. A needle in the lung will give a picture much like the above except that there will be no oscillations.

In putting air in the chest, while at the same time evacuating fluid from a cannula lower down in the chest wall, if the artificial pneumothorax needle is in the fluid, the fluid will usually appear in the glass tube near the pneumothorax needle, but it may not. If you do not get good oscillations on the negative side, then treat it as being in the fluid and clamp off your air delivery tube till you have allowed some of the fluid to be evacuated by the lower cannula. Then the introduction of some air will hasten evacuation.

It must be remembered that once air is admitted into the pleural cavity in which there is fluid, you have added to the mobility of the fluid. The latter tends to diffuse itself according to position and unless the patient is well propped up, you will not remove all the fluid, a matter of very small moment, however, unless it be purulent.

If the needle is in the pleural cavity and you have turned on the air and find that one hundred cubic centimetres have sufficed to turn a good negative into a positive pressure, you are in a pocket and have little hope of compressing the lung from that puncture; you must try elsewhere.

The pleural cavity that has some fluid in it, will act in the manner described in the last paragraph, but the pressure will not so quickly pass from negative to positive and, of course, one makes sure of the fluid by other means.

When one has felt the blunt needle or cannula or stilette against the parietal pleura and has pushed on into a cheesy resisting area of some depth, the chance of doing useful work at that spot is small.

Case Reports.

Simultaneous evacuation of fluid and filling with air has sometimes to be resorted to. This is made much easier by the use of a Burrell's evacuation bottle. The latter is a globoid, graduated bottle that can be suspended to the bedside. It is two-thirds filled with water. The upper end is connected to the cannula in the chest wall by means of a rubber tube. The other end of the rubber tube fits on to a glass tube that passes through a tightly fitting cork into the bottle. From the other end of the bottle depends a rubber tube, with a clamp, leading into a basin. The clamp may be undone to any extent and a vacuum caused in the bottle, thus procuring a gentle emptying of the chest (see Figure Ia).

Case I (see Figures II and III) shows the gradual breaking down of adhesions. These adhesions were not subjected to the pressure of large charges of air, but were bombarded with frequent moderate amounts, with very satisfactory results, the remaining apical and basal adhesions in Figure III are negligible.

Adhesions marked "+" took six refills to break down.

Case II (see Figures IV, V and VI) manifested the so-called "pleural rings." These have been mistaken for cavities, but have been demonstrated to be circular adhesions which can be broken off, the lung collapsing and leaving occasionally the semblance of the old ring still *in situ*. The rings are, as can be seen, the seat of very firm adhesions, but even these are slowly pulling apart with somewhat bigger fillings than in Case I. Very little

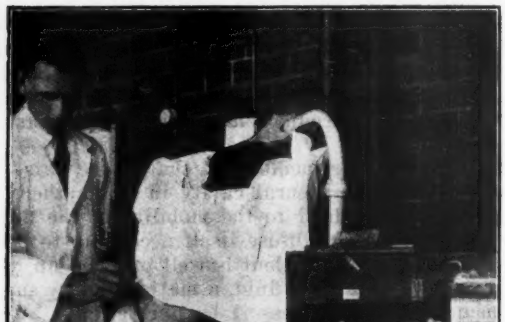

FIGURE Ia.

after-pain occurs apparently in these pleural ring cases. In Case I there was a good deal of pain that had to be controlled by morphine.

Case III was a very uninviting bilateral case, but the compression is satisfactory and the patient started to improve from the first filling. Further compression may be induced but the patient is particularly well under present conditions.

Refills.

Small amounts of air at a time and frequent repeats should be the routine procedure. When considerable adhesions are present we often refill every second day, thus keeping up a constant bombardment on the adhesions for ten days, then every third, then fifth and so on till fair collapse is obtained. Once collapse is established, the routine at Brompton is three-weekly refills. Sometimes, if there has been some difficulty in getting the needle in, the initial filling may be increased to make sure of getting in next time. In patients with hæmorrhage quick compression is indicated even at the expense of some risk from over-filling. The proper piloting of the patient after collapse is established is of great importance. The spacing of the refills is soon adjusted, but the amount of compression for any particular case is another matter.

Each patient seems to have an optimum compression point at which the sense of well-being is maximum, weight increases and sputum diminishes. Not all patients do well on a complete collapse. Indeed, some operators never aim at such a final result. Lillingston's article on "Spacing of Injections" is of great help.

Morriston Davies points out that a patient may do extremely well owing to more or less permanent adhesions, with a collapse "equal to half a lung" (see Figure XVI). This was the patient's "optimum," though there were no adhesions and complete collapse was attained.

Choice of Gas.

There has been an all-round return to air. Dr. Rolleston considers the choice of gas unimportant. Morriston Davies always uses nitrogen. Wingfield, on the other hand, thinks that pleural effusion is commoner after nitrogen.

The supposed inhibiting effect of oxygen on the growth of tuberculosis is unfounded. The habitual employment of oxygen means more frequent refills and never at any time complete collapse, owing to the greater diffusibility of this gas. The risk of gas embolism was supposed to be lessened by using oxygen. Dr. Lillingston sounds a note of warning about oxygen. He thinks it may confer a false sense of security on the operator. Probably, after emptying a chest of semi-purulent fluid, it may be advisable that the first filling should be with oxygen.

"Lipiodol."

"Lipiodol" was introduced into diagnosis of lung conditions by Armand-Delille and Duhamel some three years ago. Since that time its usefulness has been demonstrated by various clinicians in England and America.

There has been quite a difference of opinion as to the better route of introducing it. The laryngeal route demands a throat man and in his hands it is a long process and not easy. The tracheal method is simple and short and free from danger. It can be understood that a straight needle is unsuitable; a bent trocar and cannula are used. The cannula resembles a tracheotomy tube, it being fitted with side "lugs" to which tapes are attached. A means of tying in the cannula once inserted is of very great importance. Sometimes before the "Novocain" is introduced, the larynx makes desperate efforts to eject the foreign body. The patient is turned on whatever side is under investigation and his head and neck are sufficiently raised to allow an easy descent of the "Lipiodol." Six or eight cubic centimetres of 1% "Novocain" are introduced, one cubic centimetre at a time and then twenty to thirty cubic centimetres of "Lipiodol" are slowly let in. This is not followed by any discomfort. The patient is kept in this position and immediately screened and filmed. The subsequent stay in the lung does not seem to be attended by any untoward symptom; indeed, it is very soon ejected in the expectoration.

One or two points in the actual introduction of the needle may be mentioned. The site of puncture in the trachea lies between the cricoid and thyreoid cartilages. The larynx is made prominent by placing a small pillow under the shoulders and by letting the head

fall back without causing discomfort. The injection of a little "Novocain" intradermally will allow a small skin incision to be made and the trocar and cannula to be introduced. In the meantime the trachea is firmly fixed by the thumb and forefinger of the left hand and the trocar is pushed into the trachea. Being curved, its direction is downwards as well as backwards; it will not impinge on the back of the trachea.

In the following two cases "Lipiodol" was used in conjunction with artificial pneumothorax as an aid to diagnosis.

Case IV (see Figures VII, VIII and IX).—H.S., male *ætatis* fifty years, was handed over from the surgical ward for investigation as a suppurating hydatid was suspected. There was purulent sputum and foul breath, with a dark patch on the X ray film in the middle of the left upper lobe. Physical signs were dulness circumscribed over the area above indicated and coarse crepitations. It was decided to collapse the lung on to the lesion. There were extensive adhesions and collapse was slow and did not become complete. The improvement was immediate and striking. Expectoration, though present at first, soon ceased altogether; the breathing became normal; he rapidly increased in weight. By this time he was an out-patient coming up for fortnightly refills. One day he returned saying that he had had a relapse of some kind and was feeling very bad. The X ray picture was very indefinite, but certainly was not that of the partially collapsed lung of the previous fortnight. He was given twenty-five cubic centimetres of "Lipiodol" by the tracheal route and then the condition was apparent. The abscess had broken bounds. There was only one thing to do; his chest was opened and drained. The patient has made a very decided, though protracted recovery.[1]

Case V (see Figures X, XI and XII).—N.M., male, *ætatis* forty-two years, was admitted in a condition somewhat similar to that of the first patient. Fœtid breath and foul expectoration with dulness and crepitations over an area close to the mediastinum about the middle of the upper lobe of the left lung were noted. There was no history of a prior pneumonia or, indeed, of any lung condition at all. The limited area of dulness was present, definitely confirmed in the X ray picture. "Lipiodol" introduced by the trachea showed, what at first sight would appear to be a normal lung, but it will be noticed that there is a certain lack of filling corresponding to the area indicated above (see Figures X and XI). At any rate it was suspicious enough to call for a confirmatory diagnosis by collapse; a mass to the left of the mediastinum made up of uncompressible lung tissue and "Lipiodol" can be seen (see Figure XII). Here again there was considerable improvement; and the fœtid breath was disappearing, there was less expectoration and cough, the temperature was lower and there was increase of weight. In spite of that, however, surgical interference was contemplated, but the situation of the abscess was not inviting and operation was delayed. Meantime, he was so well that he was allowed to go home at his own urgent request and came up for refills. One night he was seized with severe pain in the epigastrium and was brought to the hospital. Pain was relieved by morphine and the patient was made otherwise comfortable. No extensive examination was made other than to demonstrate that while there was still a hyperresonance over the upper part of the chest, there was dulness at the base. His condition was far from critical and he was made comfortable for the night. It was proposed to examine him radiographically on the following morning and to determine what further measures should be taken. He had a violent fit of coughing in the middle of the night and died. *Post mortem* it was discovered that the abscess had burst and discharged into the pleural cavity.

Greer who has treated fourteen patients with lung abscess reports favourably of artificial pneumothorax in six.

Balboni and Churchill in the *Boston Medical and Surgical Journal* report the case of a lung abscess at the base of the right lung of a girl of eight being discharged by artificial pneumothorax so satisfactorily that the lung was collapsed for only two months and on re-expansion revealed no indication whatever of the old lesion.

Hedblom, reporting forty-eight cases from the Mayo Clinic, says that penumothorax is the treatment *par excellence* for centrally situated abscess. For any other kind he advocates either extra-pleural collapse or simple thoracotomy and drainage; he maintains that in the Mayo experience pneumothorax for a peripheral abscess is highly dangerous. One cannot expect to get drainage from that region through a bronchus and, besides there are usually many pleural adhesions to a peripheral abscess.

Whittemore in dealing with one hundred patients found artificial pneumothorax of only diagnostic value.

In the two cases recorded above the abscess in the first patient was midway between peripheral and mediastinal and in the second was wholly central. The immediate results, more sputum and then an almost complete cessation, the striking betterment of the patient with increase of weight, all lulled one in a sense of security.

Hedblom stresses the necessity of making sure of free drainage, pneumothorax, he thinks, can play its part only in presence of efficient drainage.

When one comes to consider closely the second case, it is noted that the "Lipiodol" did not indicate any large passage between a bronchus and the abscess, a circumstance that should have put us on our guard.

Needless to say it is not advisable to have the air in the chest at a great pressure; the pressure should be just enough to outline the abscess, even if it calls for frequent refills.

The conclusion seems to be that artificial pneumothorax is not to be taken by any means as a routine treatment in lung abscess.

Case VI.—I wished to demonstrate a small cavity in left apex (see Figure XIII). Figures XIV and XV depict an uninterrupted collapse with ejection of the "Lipiodol." The pictures have been transposed, the collapsed left side appearing as the right.

Case VII (see Figure XVI).—This was a case where there was some doubt as to which was the more offending side. There were fœtid breath and expectoration and considerable bilateral involvement confirmed by X ray examinations. The "Lipiodol" clearly indicates considerable breaking down of lung tissue on the right side.

[1] Since writing the above the patient has returned with signs of the old trouble, expectoration and cough. X ray examination was very indefinite. "Lipiodol" was again given intratracheally with the result seen in Figure II, a condition which calls for more drastic chest surgery.

CASE VIII (see Figure XVI).—This was of a patient sent in for collapse with the diagnosis of bronchiectasis.

Such is a brief *résumé* of the uses of artificial pneumothorax with or without "Lipiodol." No pretence is made to deal with it *in extenso* either as regards its history, uses or complications. It is a plain statement from a general hospital practice of a therapeutic measure that has been too much neglected and that should form a very important part of routine treatment of pulmonary tuberculosis.

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(9) F. Bezancon *et* L. Bernard: *La Presse Médicale*, 25 *février*, 1924, *page* 157.

DR. R. R. STAWELL (Melbourne) asked Dr. Mackeddie what happened in the case he had cited of lung abscess where surgical drainage had proved of no avail. He cited a case in his earlier experience where the bronchoscope had been successfuly used as a sound (intratracheal ether being used) in early surgical treatment of the lung. He advocated that surgery of the lung in severe cases of lung involvement was a thing to look for and tackle.

Dr. Mackeddie elaborated from further cases quoted the deceptive nature of the temporary improvement in complicated lung disease. The patient seemed well enough to be discharged, but "Lipiodol" often revealed a large unsuspected cavity; an abscess which had been accumulating, might rupture into the pleural cavity with very rapidly fatal issue. He testified further to the extreme value of "Lipiodol" in revealing cavities which X ray examination alone did not disclose.

Regarding artificial pneumothorax it was amazing how slow the advance in treatment by this method had been. Though it had been suggested in 1886, it had not been taken up at all in England until twenty years later and advance had been slow since then. There was no doubt about its efficacy. The question arose as to when it should be applied, the class of case suitable for it and the best method of introduction of the gas. He favoured the needle rather than the trocar and cannula method Air was the recognized gas, there being no advantage in the use of helium or bromoform. No danger arose of air embolism, because the gas was delivered only when it was certain that the point of the cannula had entered the pleural cavity.

SOME OBSERVATIONS ON THE EXAMINATION OF THE CEREBRO-SPINAL FLUID.

By OLIVER LATHAM, M.B. (Sydney),
Pathologist, Mental Hospital Laboratory, New South Wales.

THE experience gained during the examination of some 740 cerebro-spinal fluids since 1913 naturally influence me in attaching considerable importance to this test. Among the tests to be described that of noting the pressure and amount readily obtained during withdrawal is not the least important as an increase of these may be the only pathological phenomena discoverable, as for instance in early lead encephalitis, meningismus, sunstroke and *status epilepticus*. Dr. Prior in a recent paper has pointed out that he finds acetone at times in true and severe cases of epilepsy.

Method of Withdrawal of Cerebro-Spinal Fluid.

Rustless steel "Record" needles nine to twelve centimetres long, one millimetre thick (or more if thick pus be suspected) and with suitably ground point and stylette of correct length, are readily obtainable today. The line between the highest points of the iliac crests marks the space between the third and fourth lumbar vertebræ. In case of failure the spaces just above or below may be tried, although at times the fluid may not escape at any of these situations. This can be proved by introducing another needle at a different level and injecting saline solution. The saline fluid can be recovered in this way through the first needle. Pus may be too thick and commonly blood clots or a tag of membrane may obstruct the flow.

Pain may be due to a leakage in the *dura mater*, as evidenced by its relief after injecting saline solution intradurally; it may be relieved by phenacetin and bromides. Some prefer to puncture in the sitting posture, the patient sitting on the edge of a bed and leaning on a chair, but I often have to use the recumbent position to carry out the procedure in general paralytics; the bed should be prevented from sagging with a board beneath the mattress. The pressure should be measured by some sort of manometer with the first lot of fluid, unless there is great excess. As the pressure varies with the patient's position and height, I prefer it taken in the recumbent position. It may be gauged approximately by the fluid shooting across the bed instead of dropping ten drops or so a minute from an average needle as happens normally. In the recumbent position 130 to 150 millimetres of water would be the average pressure in the adult.(3) Naturally the operator's hands and patient are rendered sterile as well as the bottles (with glass, rubber or waxed cork stopper, not cotton wool) since a culture or vaccine may be required. Sometimes the first few cubic centimetres may be blood-stained. If so another bottle must be applied and two clear or average specimens or more if possible must be secured, because if the pressure is increased, one sample is set aside for pellicle formation and cells are best examined from the fluid withdrawn first; if the meningococcus be

present, it will die unless placed at once in the incubator or Thermos flask at 37° C..

Naked Eye Observations.

Foam lasting more than five minutes after shaking suggests an excess of protein and inflammation.

Cloudiness implies red cells or else pus cells and mononuclear cells and flakes of lymph. Red cells introduced as a result of the needle puncturing a vein sink, leaving a clear, water-white, supernatant fluid. I find that a few cells do not interfere with a diagnosis. If less than a thousand red cells per cubic millimetre were present, there would probably be only three or four white cells (which could be subtracted from the cell count) and a negligible amount of protein. This does not interfere with the Bordet-Wassermann or goldsol test.

An amber colour with or without altered or unaltered red cells suggests intracranial or spinal hæmorrhage. The blood in the cerebro-spinal fluid may come from such diverse conditions as a fractured skull, a subpial hæmorrhage, a frank cerebral hæmorrhage, an injury to the spine, a hæmorrhage into a tumour, a hæmorrhagic meningitis or subpial or intraventricular hæmorrhage in *encephalitis lethargica*. I have mistaken the latter for general paralysis of the insane even after a *post mortem* examination, but failure to obtain a Wassermann reaction together with the finding on histological examination put me right. An amber coloured specimen with excess of protein albumin but with no excess of blood suggests Froin's syndrome occurring when that part of the theca is shut off from the rest of the system. A further puncture higher up even into the *cisterna magna* and the separate examination of this fluid and a comparison with the first sometimes enables the pathologist to localize the mischief. In the first few days of infant life a blood-stained cerebro-spinal fluid may reveal a concealed birth injury affecting cerebral function.

A delicate pellicle of coagulated fibrin may be the only pathological feature noticeable except high tension; when the tension is high a few cubic centimetres of fluid should be put aside in a narrow test tube for some hours. It is common in tuberculous meningitis and by this expedient many of the tubercle bacilli are gathered together. The pellicle should then be affixed to a slide and suitably stained and examined.

Culture Methods.

Inoculation of ordinary or special media or even of animals may be done either with the fluid itself or if it be scanty with sediment after centrifugalization. I wish particularly to emphasize that the meningococcus readily dies apart from blood heat; the vessel containing it should at once be transferred to an incubator or heated "thermos" flask. It is not enough to recognize the meningococcus in smear or culture. It is necessary to type it to settle its group. At No. 1 Australian General Hospital Captain Caldwell of the Royal Army Medical Corps and I used to place the fluid taken directly on to serum agar. In a few hours it was found that some growth had generally taken place in the cerebro-spinal fluid. By mixing four separate portions with one or other of the four group sera supplied by the Medical Research Committee on a large slide and mixing thoroughly (a few drops suffice), it was usually possible by noting in which serum clumping first took place to recognize the correct group of meningococcus and to cause the correct group serum to replace the polyvalent serum already exhibited.

Naturally the pathologist should have had knowledge and experience of the complete outfit and directions supplied by the Medical Research Council.

Cell Count and Examination of Cells.

I shall commence by stating that cells seem to diminish in number either by adhering to glass containers or by autolysing.[5]

Normal fluids rarely contain more than five cells per cubic centimetre and usually two. While more than five should be considered pathological, under five are not necessarily not pathological, unless the fluid is fresh. No difficulty will be found in counting with any modern hæmocytometer by pouring about one cubic centimetre of cerebro-spinal fluid on to a clean watch glass, then taking the stain up to the 0·5 or the mark 1·0. The stain is sucked up to say the mark 1·0 and the cerebro-spinal fluid is sucked up to the 11·0 mark on the white cell pipette. The mixture is then placed in the hæmocytometer chamber in the same manner as is done with diluted blood.

The stain consists of one gramme of gentian or methyl-violet, twenty cubic centimetres of glacial acetic acid, five cubic centimetres of formalin and water to a half of a litre. The cells in the whole of the ruled area are counted. The fluid contained represents about 0.9 cubic millimetres or nine square millimetres 0·1 millimetre deep.

I prefer the deeper Fuchs-Rosenthal chamber. With practice the count can be finished within five minutes.

It is quite possible to differentiate the smaller lymphocytes from polymorpho-nuclear cells, but transitional cells and *Gitterzellen* may cause confusion because the thickness of the slide will interfere with the action of the condenser and that of the coverslip will preclude the use of an oil immersion or high class $\frac{1}{6}$ inch objective.

For better differentiation therefore some of the tinted cerebro-spinal fluid is deposited or placed on a thin coverglass, a light ring of vaseline is made on a thin slide and a thin slide is placed on to the coverslip forming the so-called Wright's chamber. On turning the specimen over it can be critically examined even with a 1/12 inch oil immersion objective. Germs readily stain as well. Lymphocytes are differentiated from yeast-like bodies by the presence of a tag of jelly-like protoplasm round the former, while beading in the protoplasm of the *Gitterzellen* is seen.

A smear of the pus present or of the centrifuged deposit may be made for the examination of the germs and cells. The material is spread on a slide with care to avoid damage; it is then dried in an incubator and is flooded with alcohol for a minute and then the alcohol is burned. This process enables

the borax methyl blue to stain both nuclei and germs clearly; they stand out on a white background, only the outline of cell body staining. I have made over seven hundred cell counts and find that the mononuclear cells predominate in most syphilitic conditions save in general paralysis of the insane during a congestive attack. Lymphocytes also predominate in encephalitic states (apart from septic states) save during the first few days and in some tuberculous states and polio-myelitis; in other conditions polymorpho-nuclear cells are the commonest.

Proteins.

The most useful test for excess of globulin is to overlay one cubic centimetre of saturated ammonium sulphate with one cubic centimetre of cerebro-spinal fluid. If a faint ring of bluish white or more commonly a frank white ring is seen against a dark background within three minutes, globulin is in excess. A modification is to compare the opacity of this mixture when shaken with that of the cerebro-spinal fluid and water. Cloudiness means a Nonne-Apelt phase I. If this is now filtered or spun in a centrifuge and one drop of 10% acetic acid added to the filtrate and boiled, precipitation implies a Nonne-Apelt phase II, that is excess of albumin. Globulin is more often increased in syphilitic con ditions and the reacting substances involved in the Bordet-Wassermann and goldsol tests are attached to the globulins. Another test that I have found almost too sensitive, but eminently useful for detection of an increase of protein is to allow a drop of cerebro-spinal fluid from a pipette to sink down through a column of 7% carbolic acid solution in water; the drop will appear surrounded by a cloud when albumin is in excess. Doubtless excess of protein partly accounts for the yellow ring formed in pathological fluids when one cubic centimetre is floated on one cubic centimetre of 1% permanganate of potash solution.

Some capital has been made out of the fact that the proteins of one disease may differ from those present in another; for instance, it has been found that on taking a cubic centimetre of cerebro-spinal fluid in two small tubes and to the first adding one cubic centimetre of 1% mercuric chloride solution and to the other one cubic centimetre of 3% sulpho-salicylic acid, but little precipitate forms, while in general paralysis of the insane and tuberculous meningitis the precipitate in the first or mercury tube is millimetres higher than the second, whereas the reverse holds good in meningococcal and septic conditions. The reading is made after twenty-four hours. I constantly use this test as well as the following for quantitative estimation of protein to note progress in patients treated for general paralysis of the insane. Two cubic centimetres of cerebro-spinal fluid are boiled with five cubic centimetres of 10% butyric acid in a test tube; one cubic centimetre of a normal sodium hydrate solution is added and the mixture is again boiled and is then transferred to a graduated centrifuge tube. In two hours the precipitate can be measured in terms of the millimetre lines or one tenth part of a cubic centimetre. Normal figures are from 0·06 to 0·2 cubic centimetre, while in general paralysis of the insane I have obtained figures up to 1·4 cubic centimetres and lower figures in other states including chronic lead poisoning. Symonds recommends strongly the addition of 0·3 cubic centimetre of 30% tri-chloracetic acid to two cubic centimetres of cerebro-spinal fluid, boiling and after a time shaking up and comparing the turbidity with standard protein so treated. I regard the butyric acid test simpler and effective. It had been stated that if to clear tuberculous meningitic fluid a few drops of a weak tenth normal sodium hydrate solution be added a turbidity is obtained, while another portion undergoes no change with weak sulphuric acid, the reverse holding with the septic conditions. I have at times got this turbidity, but the conditions were obscure and I could not probe the matter more deeply.

The Goldsol and Other Colloidal Tests.

I have not used gum mastic or gum benzoin, but having performed some 550 goldsol tests and checked the results with those obtained by the cell count, globulin test, clinical history and in syphilitic conditions with the Bordet-Wassermann tests applied to the blood and cerebro-spinal fluid, I can testify to its being the best and most constant single test of an organic lesion and at times being almost pathognostic of general paralysis of the insane.

Weston has shown us that the goldsol precipitating material is in the globulins and Wardlaw and Gray have given us the following simple and reliable method of goldsol preparation. All glassware used throughout the process must be cleansed with *aqua regia*, rinsed with tap water and then triple distilled water. The triple distilled water gradually deteriorates after the first week. It is made by redistilling ordinary distilled water after the addition of a few crystals of potassium permanganate; glass connexions are used throughout; a clean cork may be necessary, but never india-rubber, which seems to absorb ammonia or something deleterious. It is then distilled once or twice again without addition of chemicals. To prepare 0.4% saline solution triple distilled water should be used, but an old solution of 1% will do for the control. In practice a stock 10% saline solution keeps excellently. The test is carried out in the following manner. Ten test tubes of even calibre cleaned as indicated above or a multiple of ten and two more for the controls are required. From a graduated 10 cubic centimetre pipette one cubic centimetre of the 0·4 saline solution is delivered into each test tube and to the first 0·8 cubic centimetre more; to the first tube 0·2 cubic centimetre of cerebro-spinal fluid is added mixed with a pipette and teat and one cubic centimetre of the mixture is removed to the next tube on the right. The fluid is mixed; one cubic centimetre is transferred to the third tube and so on till the tenth when the withdrawn cubic centimetre is discarded.

The dilutions will thus be from 1 in 20 ranging down to 1 in 5,120. To the control (A) 1·7 cubic centimetre of 1% saline solution are added and to

control (B) one cubic centimetre of 0·4 saline solution; to every tube from a long "606" injection burette five cubic centimetres of the goldsol preparation are added. The tubes are shaken and left till the next day, although some change or indication will be evident in thirty minutes if a change is to appear.

The unchanged yellowish pink colour is recorded as 0 and complete precipitation of the celloid gold as 5; successive degrees of reduction from bluish red, reddish blue, blue and steel white are recorded as 1, 2, 3 and 4. The following types of curves appear sufficiently often to merit recognition: Curve (i) so-called "staircase"—5555443210—in general paralysis of the insane (rarely in other forms of syphilis and disseminated sclerosis). Curve (II) a pseudo-tabetic curve is represented as 2222111000; any variation between this and curve (I) may occur. Curve (III) the so-called "stepladder"—1234421000—occurs in cerebral syphilis and *tabes*, while the shifting of the greater reduction still further to the right, that is in curve (IV)—0000224554—is called "meningitic" and suggests a septic meningitis.

Every week or when required I make up my goldsol reagent. I place 100 cubic centimetres of triple distilled water in a 500 cubic centimetre flask with one cubic centimetre of a freshly prepared 1% solution of neutral potassium oxalate over a Bunsen burner and heat till boiling. Then quickly moving inside the flame, I add one cubic centimetre of 1% gold chloride solution (ordinary good photographic double salt is satisfactory), shake thoroughly and cool quickly under a tap. An inky colour is seen to shoot quickly through the liquid which changes on to purple and finally remains a sheeny yellowish pink.

Some specimens too red are too hard and will not reduce with the 1% saline solution in an hour; those a trifle bluish may be used provided the negative control be carefully examined.

If the "Targowla"[6] colloidal reaction proves its worth, its simplicity may recommend it to outside workers. Two tubes are used: the test and the control. To fifteen drops of cerebro-spinal fluid a mixture of five drops of water and 15 drops of "Elixir Paregoric" of the Belgian Pharmacopœia is added, the control being fifteen drops of elixir and twenty drops of water. A positive reaction is a precipitate in twenty-four hours.

The Bordet-Wassermann Reaction.

Time will not permit me to describe the details of the Bordet-Wassermann test. I content myself by mentioning that while I use 0·1 cubic centimetre quantities of diluted blood serum in my tests, under the same circumstances I use 0·2 cubic centimetre of diluted cerebro-spinal fluid and one cubic centimetre of undiluted fluid and 0·5% carbolic acid.

I preserve records of the response of the patient's blood serum to the Wassermann test. In the course of my work I obtained the histories of clinical signs of one hundred and eight samples of cerebro-spinal fluid, numbers 226 to 334 of this series. It was thus in my power to compare the response of the blood and of the cerebro-spinal fluid to the Wassermann test, the cell count (though as I have said the fluid was not always obtained fresh), the globulin estimation and the goldsol curve. Of the 108 patients twenty-two had no signs of syphilis and had normal reactions all through. In one patient general paralysis of the insane was diagnosed provisionally, but this was afterwards amended. Three admitted syphilis up to twenty-five years previously.

Of the remaining eighty-six, twenty-five revealed some reaction in the blood serum but nothing in the other tests. Of these two were tabetic, five had syphilis up to forty years before, one had unequal pupils one had a condition diagnosed as either general paralysis of the insane or cerebral syphilis (it remains in doubt). Of the remaining sixty-one patients the majority of whom yielded reactions right through, forty-six were supposed to exhibit signs of syphilis and in some the diagnosis of organic conditions probably due to syphilis was made.

Regarding the relative value of the various tests it may be remarked that forty-three patients with undoubted luetic histories or clinical symptoms were subjected to examination. A reaction to the Wassermann test was obtained with the blood serum of thirty-nine; a goldsol reaction was obtained with the cerebro-spinal fluid of thirty-nine. In the case of three of these patients the results of the two tests did not coincide.

While thirty-nine specimens of cerebro-spinal fluid yielded reactions to the Wassermann test, a globulin reaction was obtained with thirty-six and in twenty-five the cells were increased.

Some years ago cerebro-spinal fluid was sent to the laboratory of patients of whom it was said that while showing signs of organic brain disease, the characters of the illness differed from those of the ordinary form of general paralysis of the insane. These fluids at times yield a high cell count, an increase of globulin and a goldsol reaction and the intrathecal pressure was raised. On the other hand no reaction to the Bordet-Wassermann test was obtained either with the blood or with the cerebro-spinal fluid. It was found at the *post mortem* examination that the fluid was increased in amount and that the pia-arachnoid had a milky appearance. Careful examination of the whole brain prepared in accordance with the formol-alcohol-Nissl-Ford-Robertson method revealed that in the cortex at least the greatest reaction was seen in the deeper layers where neuronphagia was well developed (nerve cells currounded by glia or mononuclear cells). The first or molecular layer showed only the earliest signs of interstitial changes far less than those usually associated with fatal trophic changes of general paralysis of the insane.

Of course I also found greater changes in the medulla, brain stem and central nuclei especially in the blood vessels beneath various ventricles. I recognized these to be cases of *encephalitis lethargica* and have observed a few patients from the earliest beginnings to their death within three weeks.

Chlorides.

Interest attaches to the estimation of the chloride content since it is usually so constant, about 0·74

grammes per hundred cubic centimetres. However, in eighteen consecutive cases clinically diagnosed in a London hospital as tuberculous meningitis, the chlorides were found to be diminished to 0·5%.

I have obtained figures in the region of 0·6% in a few cases suspected of being tuberculous meningitis; turbidity occurred with sodium hydrate, but I was unable to get further details.

Levinson found that a most delicate test can be obtained with 0·5 cubic centimetre.

Reliable results can be obtained in the following manner: Two cubic centimetres of cerebro-spinal fluid, ten cubic centimetres of distilled water, a few drops of potassium chromate and a pinch of chalk to insure an alkaline reaction are mixed and run into a solution of silver nitrate (5·814 grammes to the litre). The end point is when the lemon colour changes to orange. Each cubic centimetre of the silver solution corresponds to one part of sodium chloride in one thousand parts of fluid.

Glucose, Urea.

For some time Dr. Prior and Dr. Evan Jones have been estimating various constituents of the cerebro-spinal fluid and we have applied to this fluid the methods of Folin and Wu.[1] [2] We have rarely obtained much satisfaction in regard to glucose content by boiling up a cubic centimetre with 0·3 cubic centimetre of Fehling's solution and noting disappearence of blue colour in the absence of sugar. However, good results are obtained in the following way. Cerebro-spinal fluid one volume, water 8·5 volumes, 10% sodium tungstate 0·25 volume and $\frac{2}{3}$ normal sulphuric acid 0·25 volume. The mixture is left at blood heat for at least fifteen minutes and then filtered or the precipitate of proteins removed by spinning. Two cubic centimetres of the clear filtrate are boiled with two cubic centimetres of Folin's copper tartrate solution for six minutes in a vessel of boiling water. two cubic centimetres of standard glucose solution being similarly treated (one part of glucose in 10,000 parts of saturated benzoic acid). The mixtures are cooled for five minutes and to each tube two cubic centimetres of Folin's new sugar reagent are added. After a few minutes the fluids are diluted to 25 cubic centimetres.[1] [2] The tints can be compared in any colorimeter, but quite an effective one can be made of two penny so-called sample tubes (flat bottomed test tubes about 12·5 centimetres by 16 millimetres wide); one is marked as standard and in it a column of about 2·5 centimetres of the standard solution is placed. About the same amount of the unknown fluid is put in the other. The tubes are tied together, wrapped in a sheet of brown paper and the colours compared by looking down the vertical tubes against bright white paper. The height of the standard over the unknown measured by callipers in millimetres multiplied by 100 gives the grammes per litre (dividing by two if two cubic centimetres of cerebro-spinal fluid have been taken). The two tubes are made to match by either adding more unknown to its tube if its colour be weaker or by adding more standard to its tube in similar circumstances; a pipette and teat are used.

Urea can be estimated by taking five cubic centimetres of the same filtrate, adding to it one cubic centimetre of Folin's urease and two drops of his pyrophosphate mixture, incubating at 54° C. for five minutes or at room temperature for an hour and adding distilled water up to twenty-three cubic centimetres. This is tossed into 2·5 cubic centimetres of Folin's modification of Nessler's solution (never the other way about). At the same time a standard is prepared of one cubic centimetre of 0·3 milligrammes of nitrogen per cubic centimetre, water to ninety cubic centimetres, and Nessler's reagent ten cubic centimetres.

These can likewise be compared in any colorimeter. If the same method is used as described for glucose estimation, fifteen multiplied by the height of the standard over that of the unknown gives the grammes of urea in a litre of cerebro-spinal fluid. The urea and glucose contents of the cerebro-spinal fluid are supposed to follow closely the corresponding contents of the blood and to rise and fall with them. However, I have usually found them from 20% to 30% less. The finding of great excess of urea in the spinal fluid should suggest uræmia as a cause for unconsciousness, while average quantities or rather more glucose should rule out meningococcal meningitis in favour of *encephalitis lethargica* in infective states.

The deductions in connexion with diagnosis derivable from these tests may perhaps be more clearly and shortly seen from a simple table while one for normals will also be included.

TABLE I.—NORMALS.

Constituent.	In Cerebro-Spinal Fluid (Grammes per Litre).	In Blood Serum (Grammes per Litre).
Organic matter	2·23	82·9
Amino acids	0·0100	0·0099
Urea	0·06 to 0·18	0·30
Urea nitrogen	0·03 to 0·09	0.15
Glucose	0·53 or more	1·0 to 1·4
Sodium chloride	7·4	5·9
Total non-protein nitrogen	0·18	0·30 to 0·40

The total nitrogen is under 0·25 grammes, while in general paralysis of the insane it nearly always exceeds 0·30 grammes in the cerebro-spinal fluid.

One should remember that while preservatives like sodium fluoride five parts and thymol one part mixed together and added to make from 1% to 2% with cerebro-spinal fluid may preserve glucose, it may inhibit urease action.[7]

References.

[1] Some Observations on Folin and Wu's "Method of Blood Analysis," Supplement to THE MEDICAL JOURNAL OF AUSTRALIA, June 14, 1924.

[2] Myers "Practical Chemical Analysis of Blood," second edition.

[3] Levinson, "Cerebro-Spinal Fluid."

[4] Greenfield and Carmichael also give most up-to-date notes on differential diagnosis from the various analyses.

[5] Sahli, Webster, Stitt and numerous authorities on pathological methods and Symonds in *The Clinical Journal*, from 1924-1926.

ILLUSTRATIONS TO THE ARTICLE OF DR. NEIL GUTHRIE ON "THE X RAY EXAMINATION OF INTRATHORACIC AND SUBDIAPHRAGMATIC HYDATID DISEASE AND ITS COMPLICATIONS."

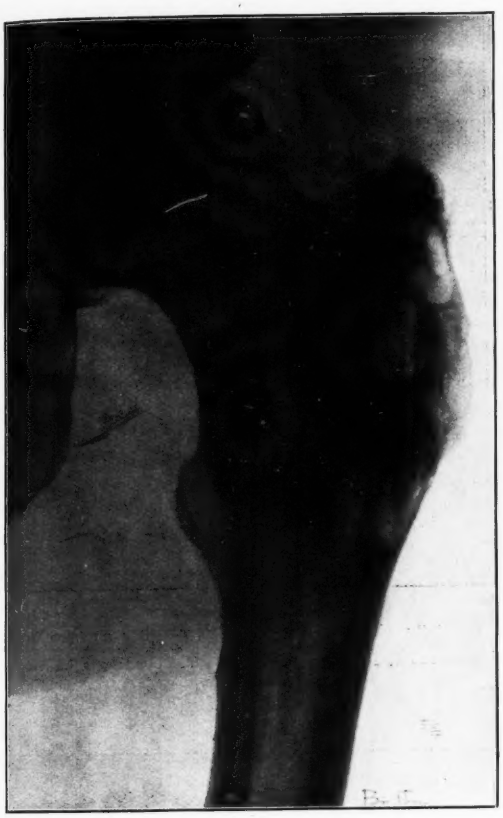

FIGURE I.
Hydatid disease in bone.

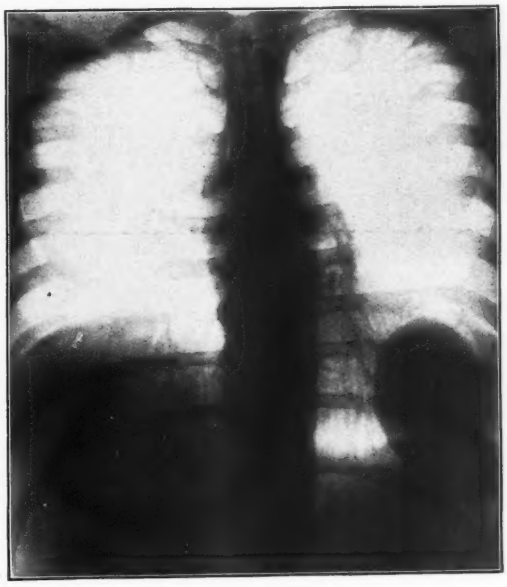

FIGURE II.
Cyst lying behind heart; defined by over-exposure for pulmonary detail.

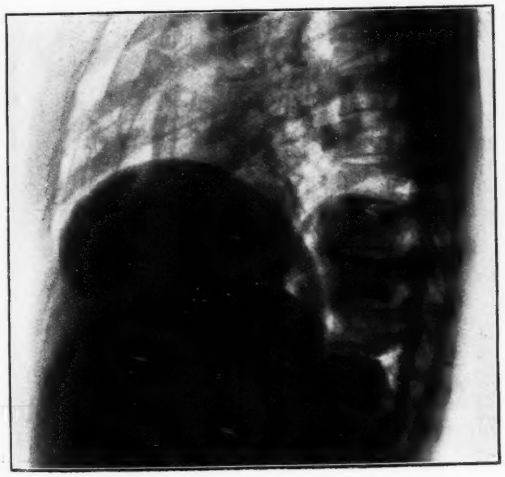

FIGURE III.
Cyst lying between the liver and diaphragm; right lateral view.

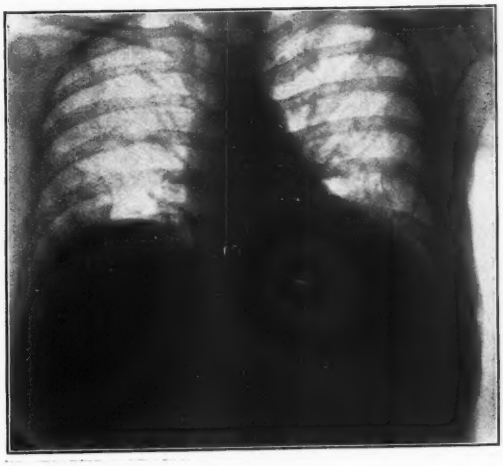

FIGURE IV.
Same case as in Figures II and III. Bilateral hydatid disease; intrathoracic cyst on the left side. Subdiaphragmatic cyst on the right side. Periphery of the shadow of the cyst continuous with the contour of the left ventricle; appearances in this exposure for pulmonary diagnosis simulate an enlargement of the left side of the heart.

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ILLUSTRATIONS TO THE ARTICLE OF DR. NEIL GUTHRIE ON "THE X RAY EXAMINATION OF INTRATHORACIC AND SUBDIAPHRAGMATIC HYDATID DISEASE AND ITS COMPLICATIONS."

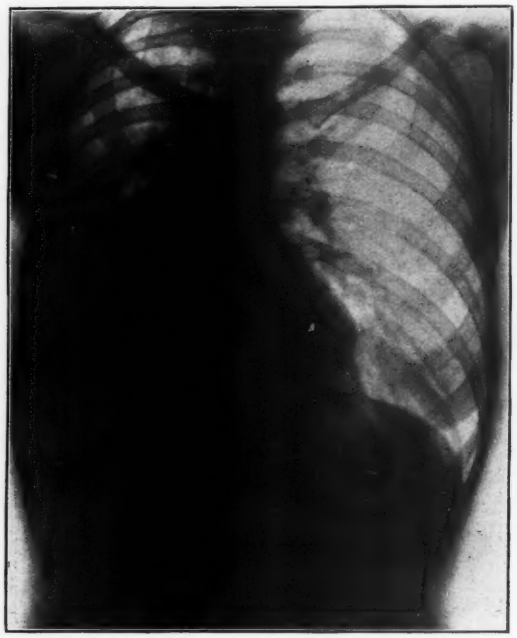

FIGURE V.
Rupture of cyst into bronchus of long standing (probably five years); fibrosis causes traction of the mediastinal structures and heart to the right; pleural and pulmonary disease obscures the cyst which was localized at operation and removed.

FIGURE VI.
Partially collapsed cyst on the left side; rupture into the bronchus; cicatrization of the left apex from a previous hydatid cyst which was removed by operation.

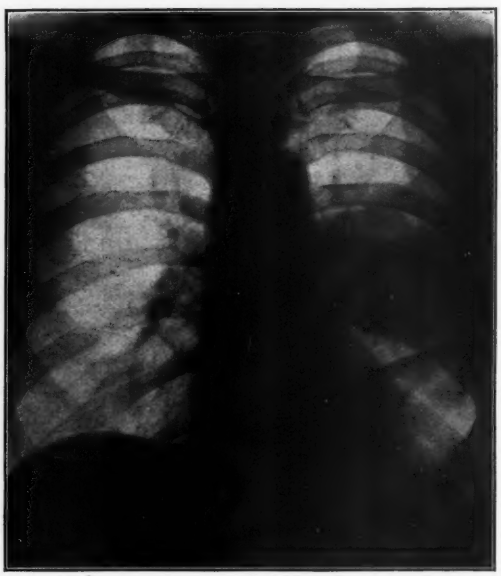

FIGURE VII.
Encapsuled pleurisy. Note the similarity to Figure VI. Hydatid disease was excluded through X ray examination of chest having been conducted two months previously with negative findings. Hydatid disease was suspected on account of eosinophilia which was probably due to psoriasis.

FIGURE VIII.
Calcified hydatid cyst of the left lobe of the liver; barium filled stomach; lateral view.

ILLUSTRATIONS TO THE ARTICLE OF DR. J. F. MACKEDDIE ON "ARTIFICIAL PNEUMOTHORAX WITH AND WITHOUT 'LIPIODOL' IN DIAGNOSIS AND TREATMENT OF LUNG CONDITIONS."

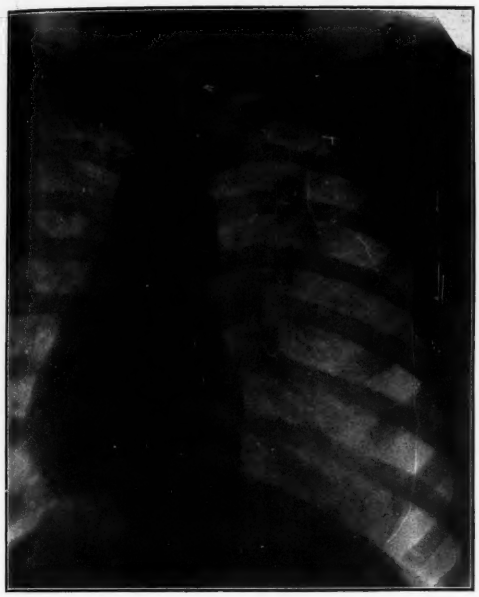

FIGURE II.

FIGURE III.

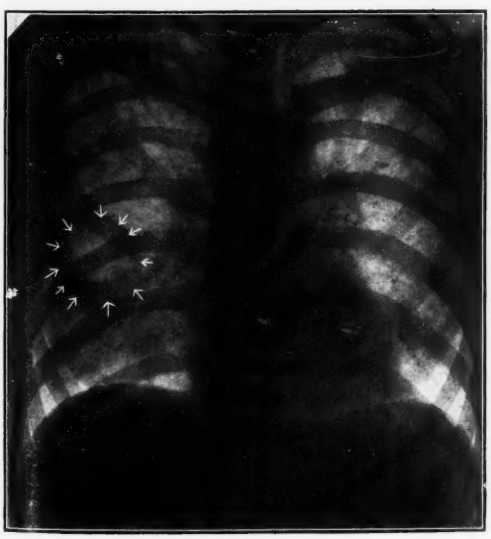

FIGURE IV.

FIGURE V.

ILLUSTRATIONS TO THE ARTICLE OF DR. J. F. MACKEDDIE ON "ARTIFICIAL PNEUMOTHORAX WITH AND WITHOUT 'LIPIODOL' IN DIAGNOSIS AND TREATMENT OF LUNG CONDITIONS."

FIGURE VI.

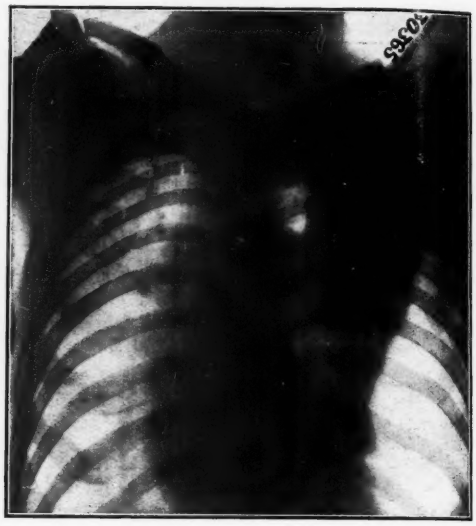

FIGURE VII.

FIGURE VIII.

FIGURE IX.

ILLUSTRATIONS TO THE ARTICLE OF DR. J. F. MACKEDDIE ON "ARTIFICIAL PNEUMOTHORAX WITH AND WITHOUT 'LIPIODOL' IN DIAGNOSIS AND TREATMENT OF LUNG CONDITIONS."

FIGURE X.

FIGURE XI.

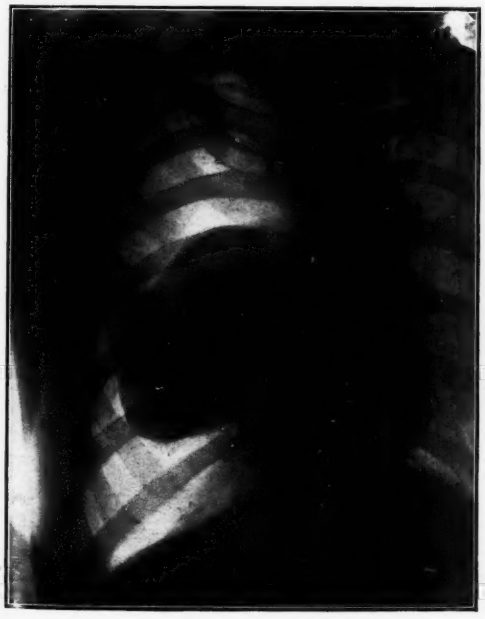

FIGURE XII.

FIGURE XIII.

ILLUSTRATIONS TO THE ARTICLE OF DR. J. F. MACKEDDIE ON "ARTIFICIAL PNEUMOTHORAX WITH AND WITHOUT 'LIPIODOL' IN DIAGNOSIS AND TREATMENT OF LUNG CONDITIONS."

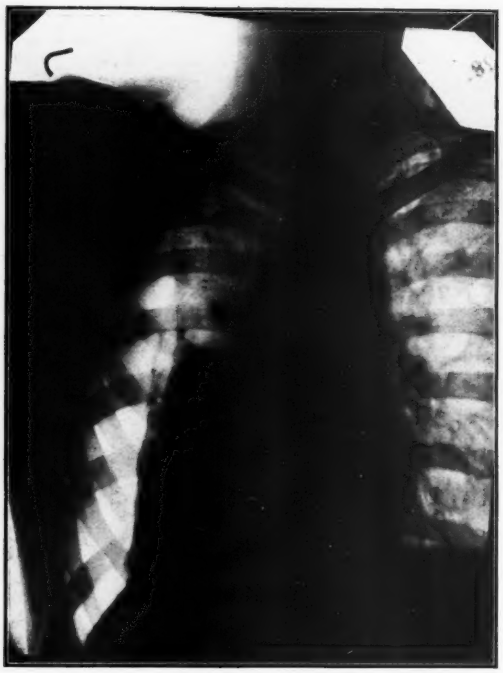

FIGURE XIV.

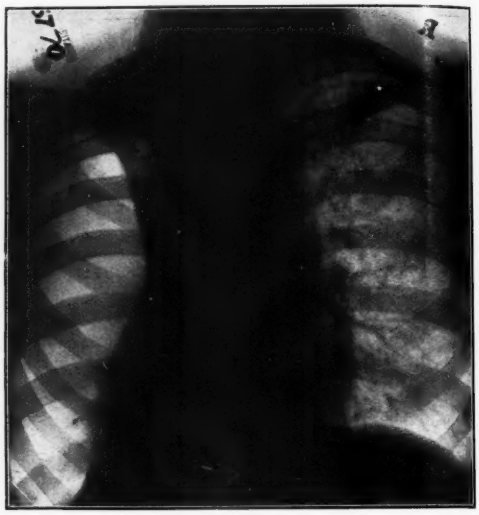

FIGURE XV.

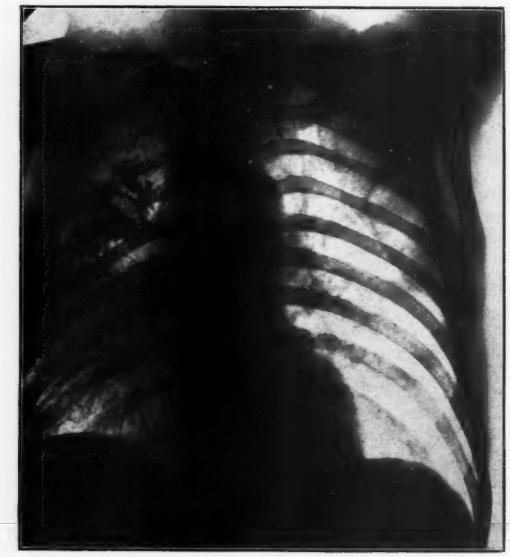

FIGURE XVI.

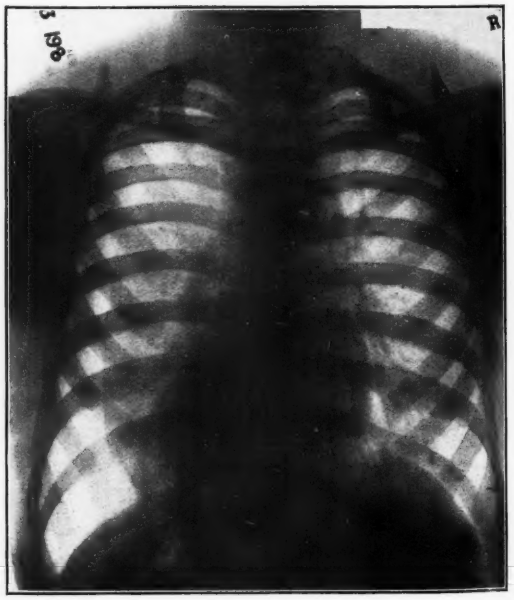

FIGURE XVII.

ILLUSTRATIONS TO THE ARTICLE OF MR. R. GORDON CRAIG AND DR. R. K. LEE BROWN ON "THE SURGERY OF EPITHELIAL BLADDER TUMOURS."

FIGURE I.
Grade 1: Epithelial cells practically all well differentiated.

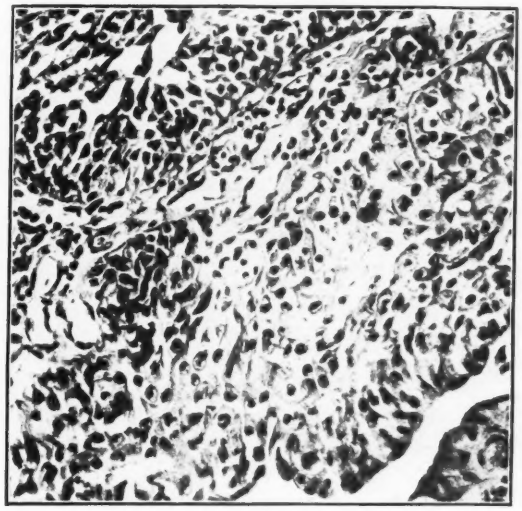

FIGURE II.
Grade 2: Differentiated and undifferentiated epithelial cells about equal.

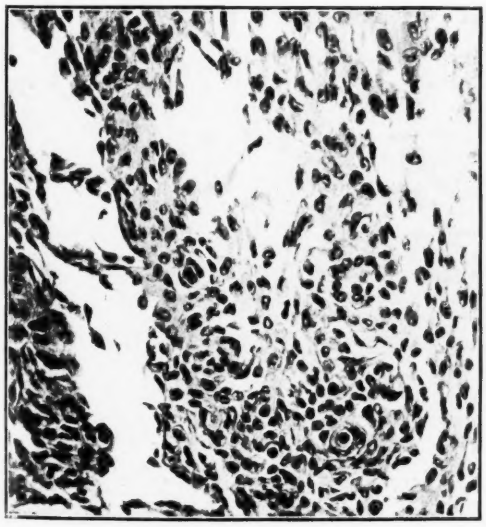

FIGURE III.
Grade 3: Epithelial cells, three-quarters undifferentiated, one-quarter differentiated.

FIGURE IV.
Grade 4: Epithelial cells practically all spherical and undifferentiated.

ILLUSTRATIONS TO THE ARTICLE OF DR. A. H. TEBBUTT AND DR. V. R. WOODHILL ON "TUMOURS OF THE THYREOID GLAND."

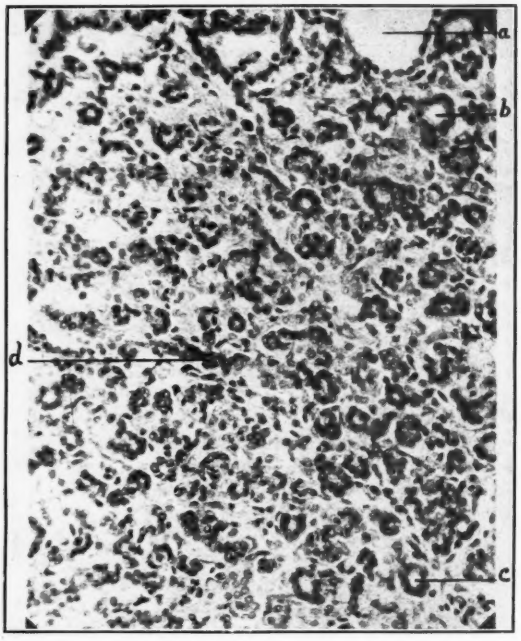

FIGURE I.
Thyreoid of a human embryo, greatest length 54 mm., for comparison with adenomata. *a*, Large alveolus; *b* and *c*, small alveoli; *d*, column of cells. × 250.

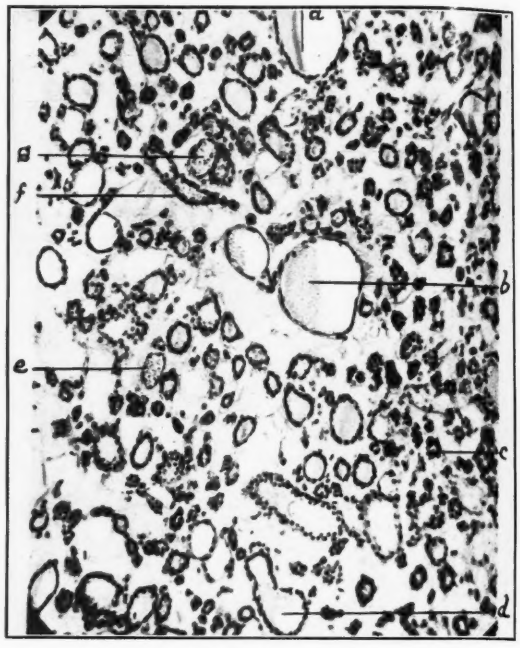

FIGURE II.
Adenoma: Case I. *a* and *b*, Larger alveoli with some colloid; *c*, minute alveolus; *d*, appearance of budding alveolus; *e* and *g*, thin walled blood vessels; *f*, tubular alveolus. × 120.

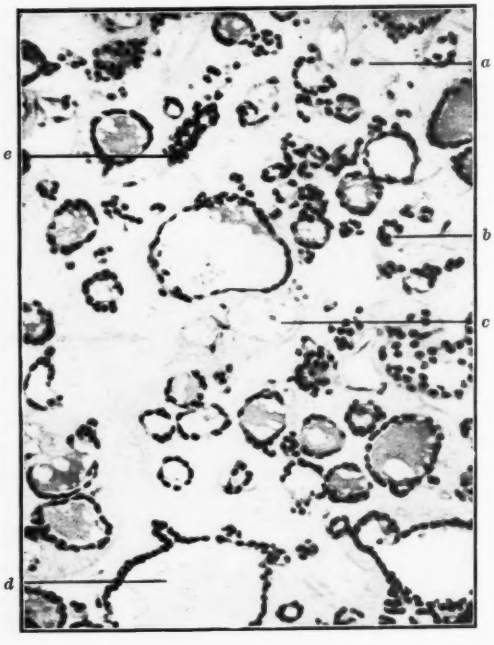

FIGURE III.
Adenoma: Case II. *a*, So-called hyaline degeneration of stroma; *b*, minute alveolus; *c*, thin walled blood vessel; *d*, large alveolus with colloid; *e*, column of cells. × 250.

FIGURE IV.
Adenoma: Case III. Size of hen's egg; cut surface after bisection, showing central hæmorrhages.

FIGURE VI.
Adenoma: Case IV. Size of small orange; cut surface showing capsule, fissures and hæmorrhages.

ILLUSTRATIONS TO THE ARTICLE OF DR. A. H. TEBBUTT AND DR. V. R. WOODHILL ON "TUMOURS OF THE THYREOID GLAND."

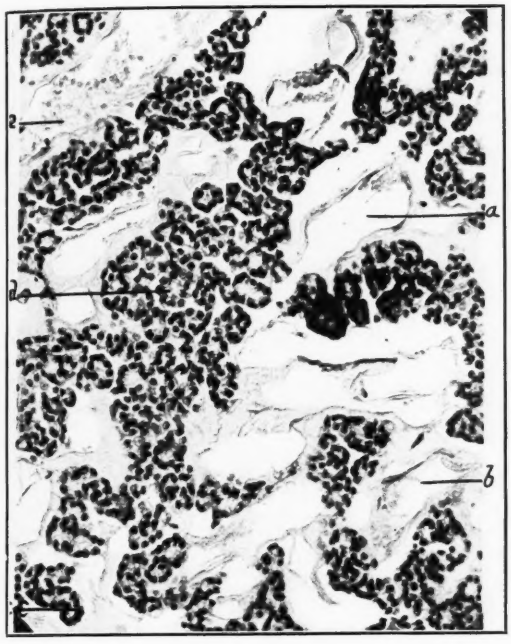

FIGURE V.
Adenoma: Case III. *a*, *b* and *e*, Thin walled blood vessels; *c*, tubular alveolus; *d*, group of alveoli or possibly cross section of twisting tubules. × 250.

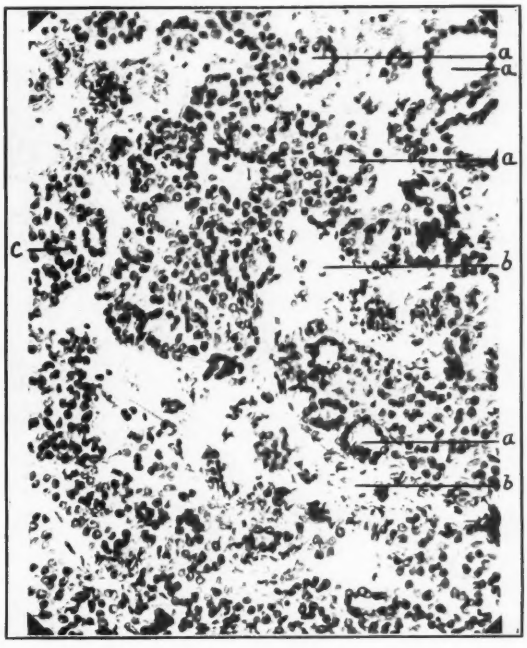

FIGURE VII.
Adenoma: Case IV. *a*, Small alveoli containing pale colloid; *b*, spaces containing red blood cells; *c*, cluster of thyreoid cells. × 250.

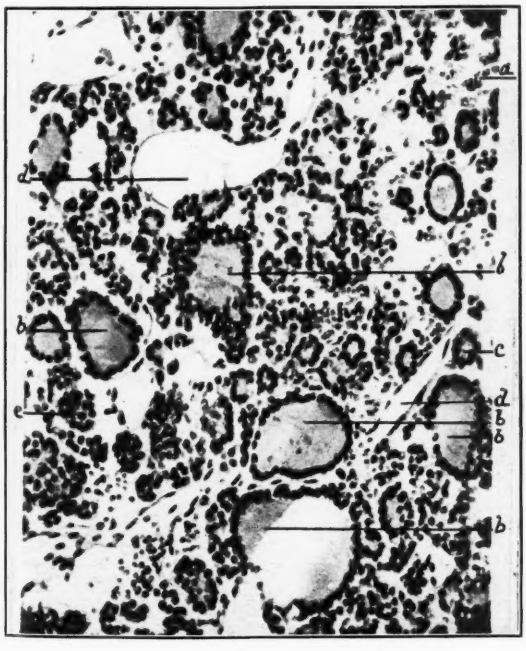

FIGURE VIII.
Adenoma: Case V. *a*, Red blood cells; *b*, alveoli containing colloid; *c*, small alveolus; *d*, blood vessel with only endothelial lining; *e*, cluster of thyreoid cells. Note the absence of basement membrane. × 250.

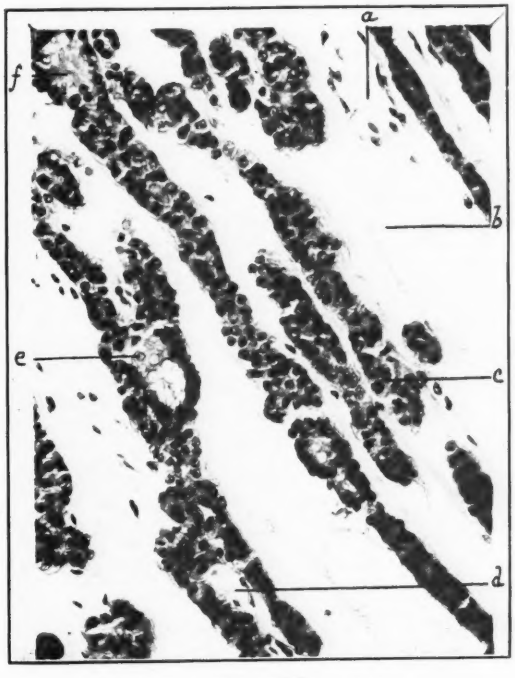

FIGURE IX.
Adenoma: Case VI. *a* and *b*, Blood vessel with only endothelial lining; *b*, loose, delicate stroma hardly seen; *c*, columns and tubules; *e* and *f*, colloid in tubule. × 250.

ILLUSTRATIONS TO THE ARTICLE OF DR. A. H. TEBBUTT AND DR. V. R. WOODHILL ON "TUMOURS OF THE THYREOID GLAND."

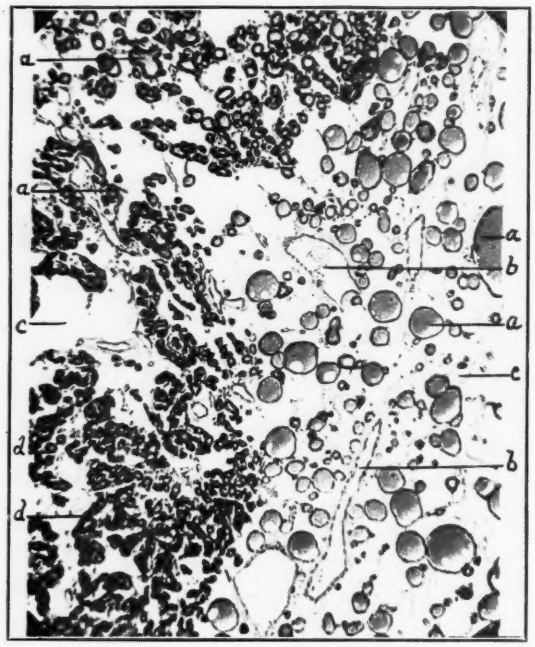

FIGURE XI.
Adenoma: Case VII. *a*, Medium and small colloid alveoli; *b*, thin walled blood vessels; *c*, ill defined stroma; *d*, small alveoli, tubules and columns. × 60.

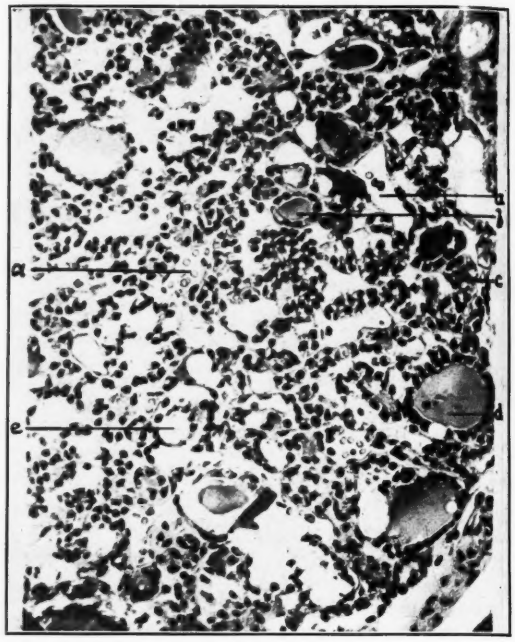

FIGURE XIII.
Adenoma: Case VIII. *a*, Thin walled blood vessel; *b* and *d*, colloid containing alveoli; *c*, groups and columns of thyreoid cells; *e*, alveolus without colloid. × 250.

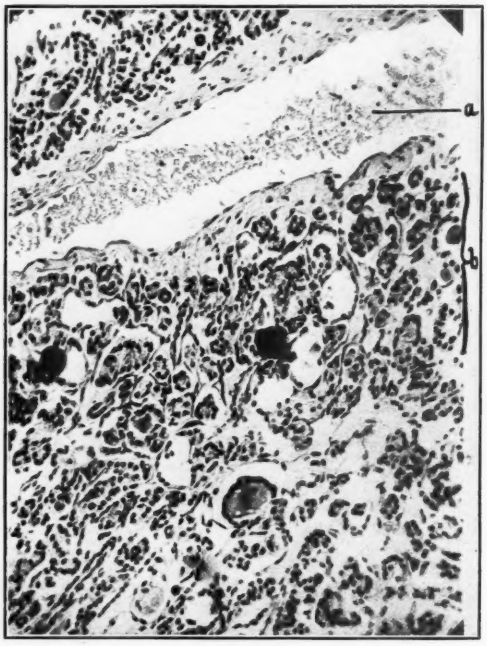

FIGURE XIV.
Adenoma (? carcinomatous change): Case IX. *a*, Large vessel; *b*, small alveoli, solid groups of cells and occasional colloid. × 120.

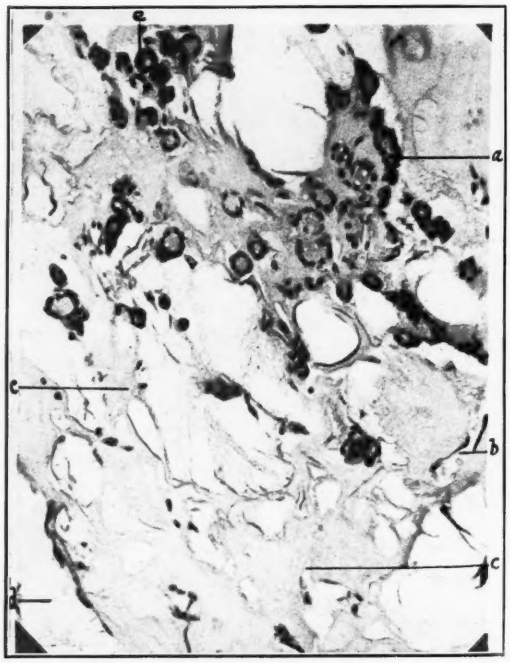

FIGURE XV.
Adenoma: Case X. *a*, Tubular alveolus; *b* and *d*, thin walled blood vessels; *c*, degenerate stroma; *e*, minute alveoli. × 250.

ILLUSTRATIONS TO THE ARTICLE OF DR. A. H. TEBBUTT AND DR. V. R. WOODHILL ON "TUMOURS OF THE THYREOID GLAND."

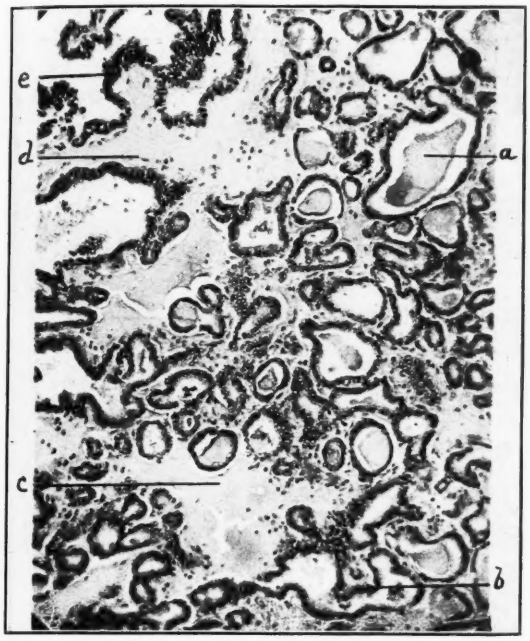

FIGURE XVI.
Adenoma (papillary tendency): Case XI. *a*, Growing alveolus containing colloid; *b*, early stage of papillary formations; *c*, interstitial colloid; *d*, degenerate stroma; *e*, later stage of papillary formations. × 120.

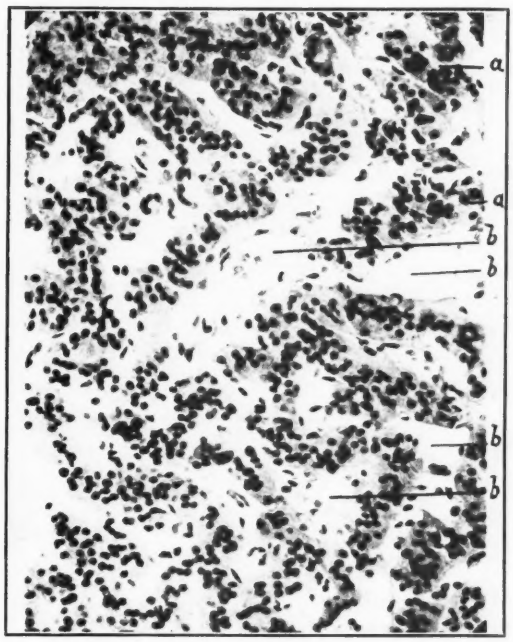

FIGURE XVIII.
Adenoma (thyreoid or ? parathyreoid): Case XII. *a*, Columns of epithelial cells between which are *b*, endothelial tubes (blood capillaries). × 250.

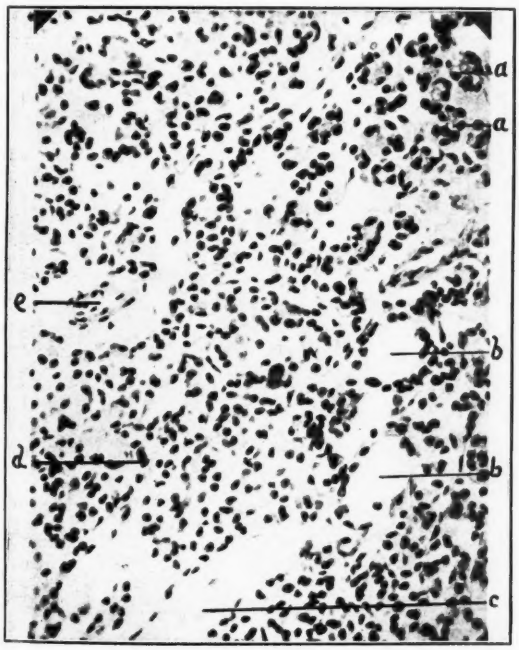

FIGURE XIX.
Adenoma (probably thyreoid): Case XIII. *a*, Small cell clusters tending to form minute alveoli; *b*, small definite alveoli with no apparent colloid; *c*, fibrous tissue; *d*, large clusters of thyreoid cells; *e*, blood vessel. × 250.

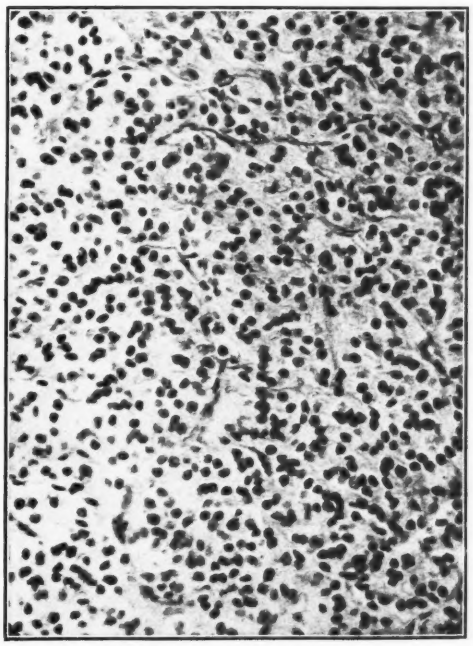

FIGURE XX.
Adenoma (probably parathyreoid): Case XIV. Cell groups separated by connective tissue containing capillary blood vessels; no alveoli. × 250.

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ILLUSTRATIONS TO THE ARTICLE OF DR. A. H. TEBBUTT AND DR. V. R. WOODHILL ON "TUMOURS OF THE THYREOID GLAND."

FIGURE XXI.
Adenoma of pancreas. *a*, alveolus or acinus; *b*, column of cells; *c*, delicate stroma; *d*, capsule. ×120.

FIGURE XXII.
Carcinoma of thyreoid: Case I. *a*, Fibrous stroma; *b*, small drop of colloid in a cell mass; *c*, compact cell mass; *d*, colloid alveolus with columnar epithelium. ×250.

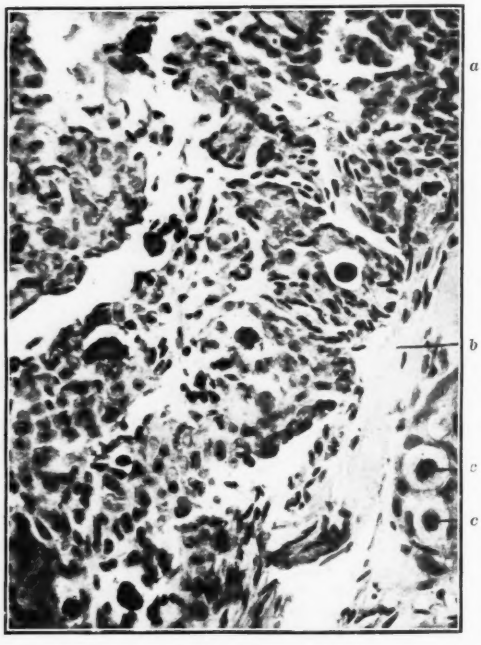

FIGURE XXIII.
Metastasis in posterior triangle: Case I. *a*, Compact cell masses; *b*, fibrous stroma; *c*, deeply staining colloid in the cell masses. ×250.

FIGURE XXIV.
Metastasis in posterior triangle: Case I. Low power view. *a*, Well formed fibrous stroma; *b*, hæmorrhage; *c*, masses of carcinoma cells. ×60.

ILLUSTRATIONS TO THE ARTICLE OF DR. A. H. TEBBUTT AND DR. V. R. WOODHILL ON "TUMOURS OF THE THYREOID GLAND."

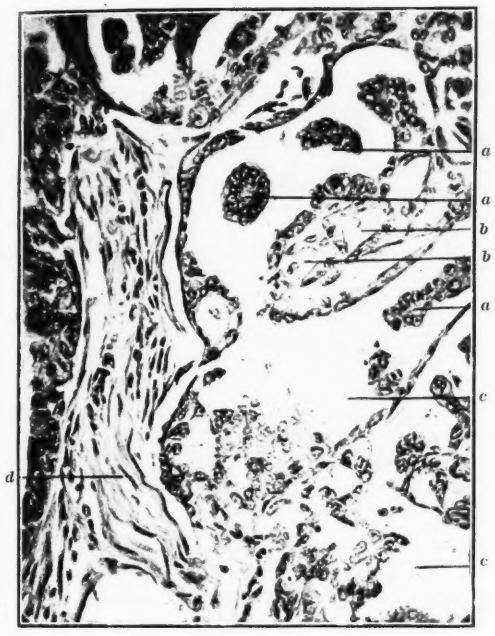

FIGURE XXV.
Papillary Adeno-carcinoma: Case II. *a*, Papillary processes; *b*, small alveoli in a papillary process; *c*, irregular spaces without colloid; *d*, fibrous band. × 250.

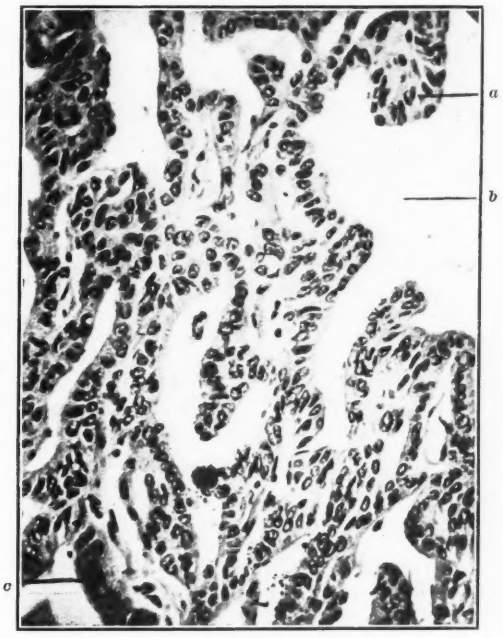

FIGURE XXVI.
Papillary Adeno-carcinoma: Case III. Section of a complex papillary process in which are irregular alveoli; no stainable colloid. × 250.

FIGURE XXVII.
Metastasis in lung: Case III. Diffuse infiltration, very different from primary growth. The pointers indicate the larger malignant cells. × 250.

FIGURE XXVIII.
Papillary Adeno-carcinoma (? papillary adenoma): Case IV. *a*, Complex papillary process containing *b*, a colloid vesicle; *c*, deeply staining columnar epithelium; *d*, the cystic space. × 120.

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ILLUSTRATIONS TO THE ARTICLE OF DR. A. H. TEBBUTT AND DR. V. R. WOODHILL ON "TUMOURS OF THE THYREOID GLAND."

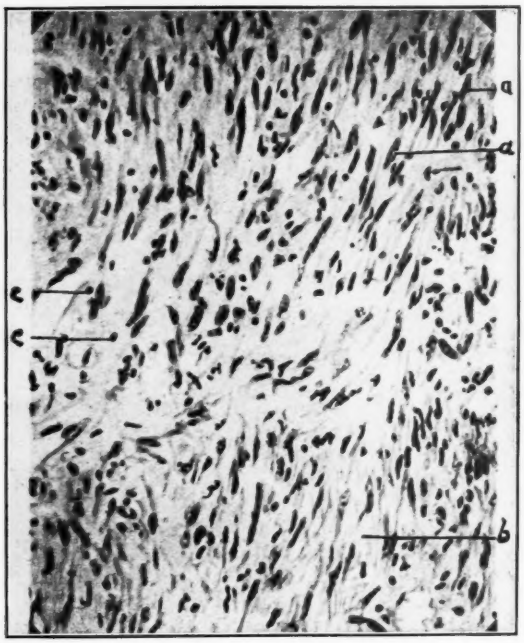

FIGURE XXIX.
Fibro-sarcoma: Case V. *a*, spindle cells; *b*, fibrous tissue; *c*, small round cells. × 250.

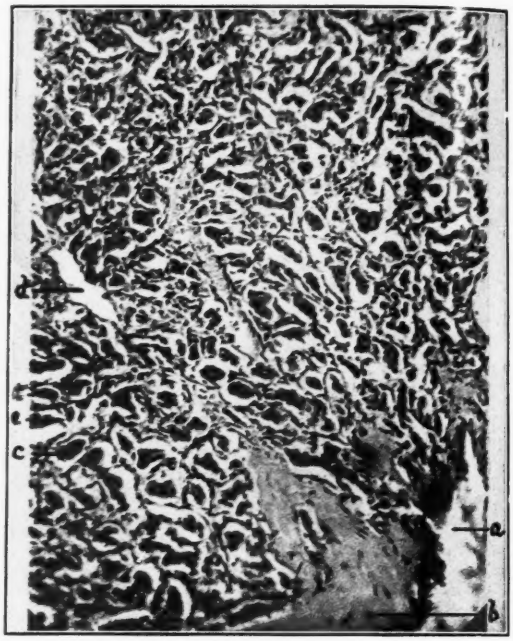

FIGURE XXX.
Tumour about the site of the carotid body. *a*, Large blood sinus; *b*, fibrous tissue band; *c*, syncytial cell cell masses; *d*, thin walled blood vessel. × 120.

ILLUSTRATIONS TO THE ARTICLE OF DR. A. H. TEBBUTT AND DR. V. R. WOODHILL ON "ABERRANT THYREOID TISSUE."

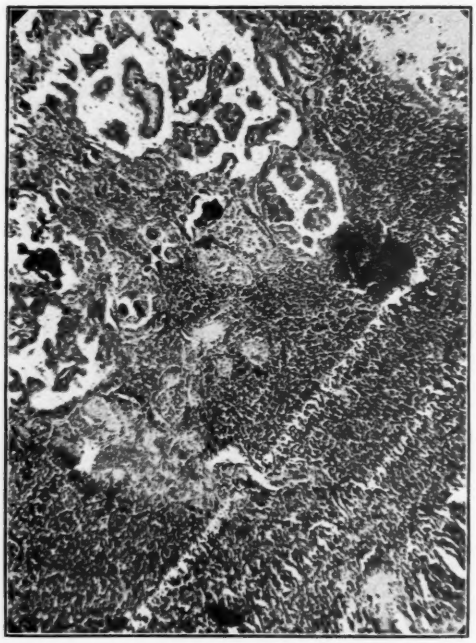

FIGURE V.
Case I: Low power view showing lymphoid tissue containing cystic spaces lined by epithelium forming papillary processes and containing in places colloid. The dark amorphous masses may be calcific colloid. × 60.

FIGURE VI.
Case I: High power view showing epithelial cell masses in the wall of cystic spaces and central papillary process with colloid just beneath it. Lymphocytes in one corner. × 250.

ILLUSTRATIONS TO THE ARTICLE OF DR. A. H. TEBBUTT AND DR. V. R. WOODHILL ON "ABERRANT THYREOID TISSUE."

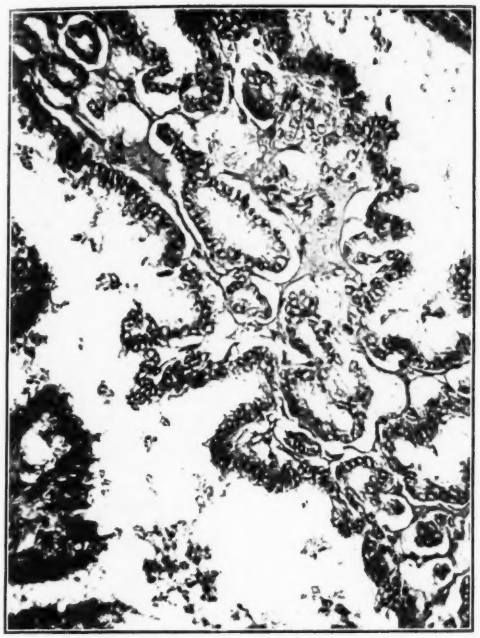

FIGURE VII.
Case I: Another nodule showing marked papillary formations with columnar epithelium and alveoli in the papillæ. Colloid appears to be interstitial. Malignancy suggested by histology.

FIGURE IX.
Case II: Supraclavicular nodule showing papillary formations in cystic spaces containing colloid in places. × 250.

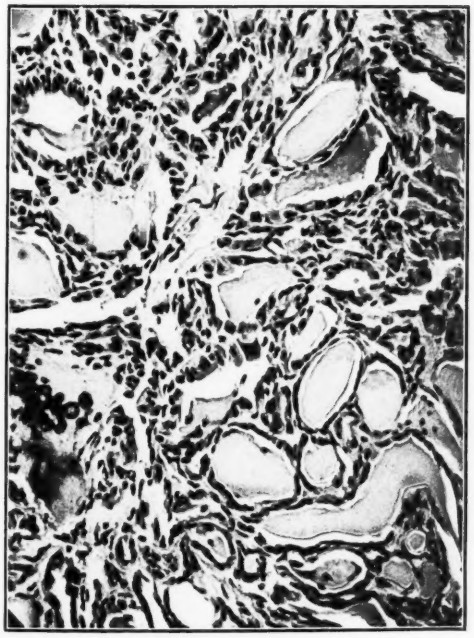

FIGURE X.
Case II: Nodule high up in the neck. Colloid alveoli and tubules, but also intervening columns suspiciously like carcinoma. The cluster of dark rounded bodies at one margin appears to be calcific deposit. × 250.

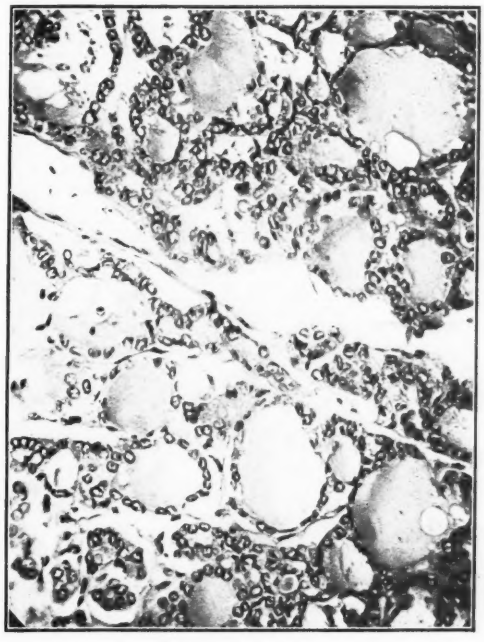

FIGURE XII.
Case III: This shows a non-papillary area, but resembling one form of adenoma. × 250.

ILLUSTRATIONS TO THE ARTICLE OF DR. A. H. TEBBUTT AND DR. V. R. WOODHILL ON "ABERRANT THYREOID TISSUE."

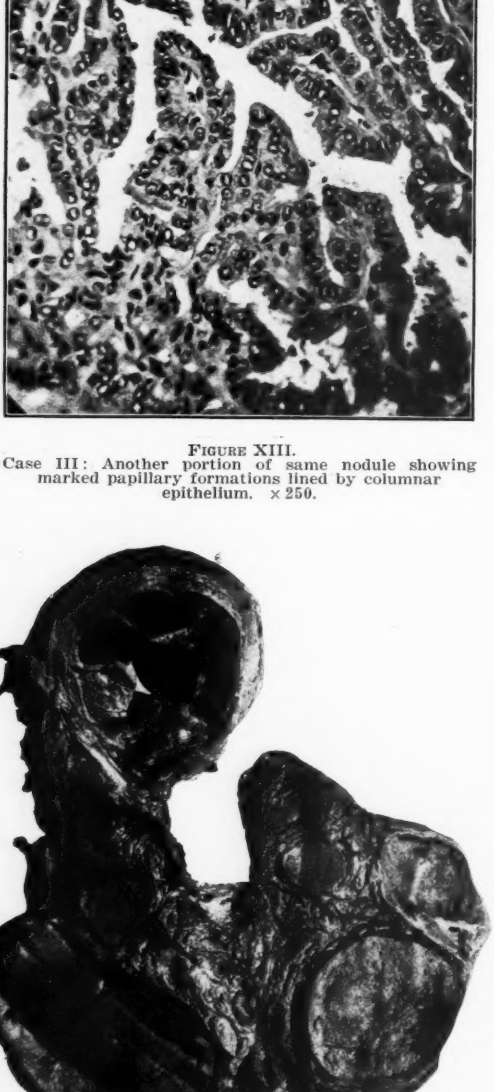

FIGURE XIII.
Case III: Another portion of same nodule showing marked papillary formations lined by columnar epithelium. × 250.

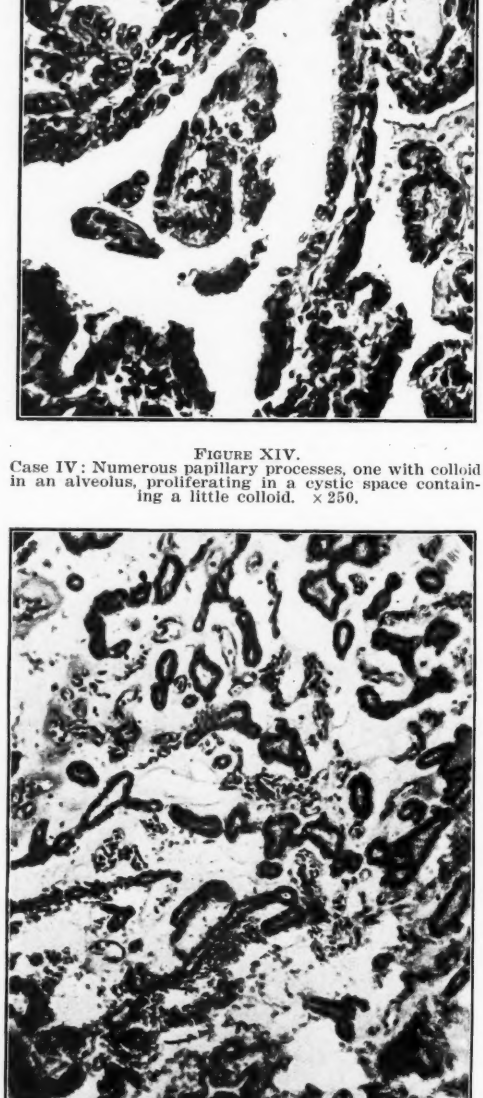

FIGURE XIV.
Case IV: Numerous papillary processes, one with colloid in an alveolus, proliferating in a cystic space containing a little colloid. × 250.

FIGURE XV.
Case V: Multiple adenomata, one cystic, but not papillary. Juvenile myxœdema. A different type of case from numbers I to IV, but belongs to the category of tumours of aberrant tissue.

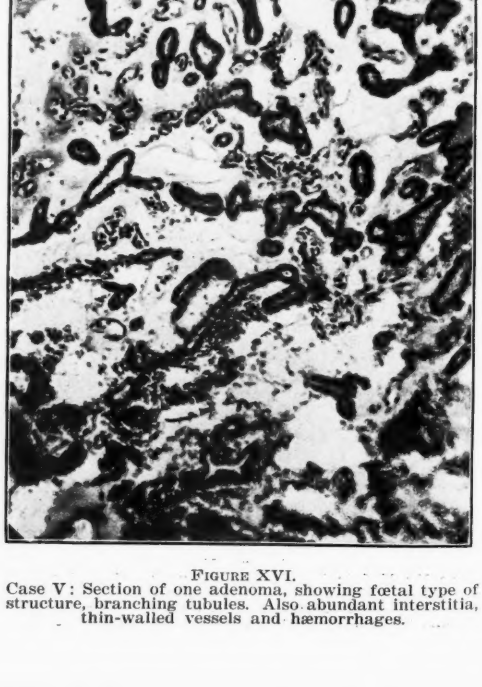

FIGURE XVI.
Case V: Section of one adenoma, showing fœtal type of structure, branching tubules. Also abundant interstitia, thin-walled vessels and hæmorrhages.

(6) *The Lancet*," October 31, 1925, page 929.

(7) B. Splatt, "A Note on the Preservation of Samples of Blood for Sugar Estimations," The Medical Journal of Australia, August 7, 1926, page 178.

(8) Beaumont and Dodds: "Recent Advances in Medicine: Clinical, Laboratory, Therapeutic."

Section II.—Surgery.

THE SURGERY OF EPITHELIAL BLADDER TUMOURS.

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That cancer of the bladder is an incurable disease is a statement that has stood unchallenged until recent times, well within the memory and experience of some senior surgeons who are living and at work today.

Until this century there was no darker page in the history of surgery than that concerning the malignant tumours of the bladder. Light, however, has been thrown on this darkness, particularly during the last fifteen years. Before this time these tumours had to be felt to be recognized, but now with improved methods of endoscopic examinations, we do not need to wait until we can feel them; we can actually see them in their earliest stages. The profession and through them the public are slowly recognizing that blood in the urine is a serious symptom and is often the first sign of a bladder growth.

The object of this paper is to give a short outline of the history of surgical progress in dealing with epithelial bladder tumours, with special reference to the last fifteen years, based on a series of one hundred and fifty-four cases spread over that period.

History.

Tumours of the bladder were described as early as 1551. Even up to the middle of last century, however, there was little knowledge of or interest taken in this subject except in the *post mortem* room. One writer in 1850 said that: "Malignant disease of the bladder is relievable only by opiates and the less done, the better for the patient." It remained for an Englishman, Sir Henry Thompson, the father of British urology, to break away from this accepted belief.

In 1880 while he was crushing a stone, he caught in the blades of his instrument something that was anchored to the bladder wall; he recognized that it must be a tumour growing from the vault of the bladder. He deliberately planned a method of attack through a median perineal cystotomy. Aided by the hand of an assistant pressing over the region of the bladder, he felt the growth with his finger and described the experience in the following words: "I soon detected the tumour of polypoid form, coming down from the top of the bladder, apparently about the size of a large filbert nut, coated with calcareous material. I then introduced a small lithotomy forceps and twisting the mass with great caution, separated the attachment and brought it away entire without difficulty."(1) This patient was living and well eight years after.

Encouraged by this result, he developed special instruments for the removal of bladder growths. Amongst the older instruments of our teaching hospitals may be found a few of these special *rongeur* forceps. In principle they are lithotomy forceps with one edge of each blade serrated, the serrated edge of each blade articulating with its fellow. He soon abandoned the perineal route and developed the suprapubic. This latter route gave him the additional advantage of sight as well as touch.

In 1888 when delivering his series of lectures upon urinary diseases, he summed up his attitude towards bladder growths in the following words (2): "We have to remember that every patient with a bleeding vesical tumour eventually succumbs sooner or later to his fate, unless surgical aid is afforded." A statement that is as true today as it was then.

French surgeons followed Thompson both as to the suprapubic route and the special instruments that he used. They did something more, however; to the use of the special forceps they added that of the thermocautery. This addition of heat for the destruction of the tumour cells was the forerunner of our present day methods, the only difference being in the method of the generation of the heat.

When we remember that up to this time, about 1890, the cystoscope was little more than a scientific toy, it is easy to realize that none but advanced cases of bladder tumour could be recognized by the *tactus eruditus* of even the most experienced surgeon. From this date rapid developments took place in the design and use of the observation cystoscope, soon to be converted into an operating instrument by the addition of the "deflecting finger" of Albarran.

In 1897 Nitze published a large series of cases in which the removal of the bladder tumours had been accomplished by means of special forceps designed by him for use through the operating cystoscope.

Our next advance came from the other side of the Atlantic, when Edwin Beer, of New York, in 1910 destroyed for the first time bladder papillomata under visual control by means of heat generated by the high frequency current. This current was conveyed to the growth by means of an insulated flexible wire passed like a ureteral catheter through the channel of the operating cystoscope.

His original method of supplying the heat differed in some respects from our method, for he used the monopolar high frequency current of Oudin, whereas now in all the great clinics of urology the bipolar current of d'Arsonval is used. Otherwise the treat-

ment for bladder papillomata is still applied in accordance with Beer's technique and his discovery must still be regarded as one of the most important additions to the surgery of the twentieth century from the point of view of the actual saving of life and the relief of suffering. The treatment of bladder tumours is characterized by wide diversity of opinion between different clinics and even between different surgeons of the same clinic. The treatment of these tumours on broad surgical lines by partial or even total excision of the bladder has been strongly advocated by surgeons of high repute and as strongly condemned by others equally distinguished; but on one point there is no dissentient voice, namely that the high frequency generation of heat in the tissues, or diathermy as it is called, is firmly established as a method of treatment of all early papillomatous tumours of the bladder.

Of the other methods of treating these tumours radium and X rays have been successfully applied for many epitheliomatous growths of the skin, but their position in the treatment of bladder tumours has yet to be defined. We are not yet in our clinic in possession of a sufficient quantity of radium to give any opinion of its value in the treatment of epithelial bladder growths from our own personal experience. In the near future we hope to be in possession of sufficient radium to enable us to apply some of the knowledge gained from the work of other surgical centres. Although personally we cannot speak of its use, we have observed some of the dangers of its use by others. We have seen an actual hole burnt through the bladder into the rectum by the over action of the radium. The suffering of this patient was intense, fortunately death supervened after months of constant pain. We have also seen several examples of radium burns of lesser degree, also accompanied by months of suffering.

Our experience of X rays is limited to deep therapy applied by colleagues versed in that branch of therapeutics. So far we cannot record a cure. Rather has it added to the sufferings of the patients, owing to severe skin reactions in the region of the sacrum and buttocks. Bed sores developed in these patients, which in our opinion would not have developed had no X ray therapy been used. An observation of interest was made in one patient who was suffering from a recurrent carcinoma in the vault of the bladder. This recurrent growth had ulcerated and was bleeding freely. Under the influence of X ray therapy this malignant ulcer healed and disappeared. But, while this reparative process was going on in the bladder, the malignant growth was rapidly extending in the tissues outside the bladder.

Nevertheless there are possibilities in X ray treatment. Physicists have discovered that the Röntgen ray is not a simple, but a complex ray made up of units of widely different wave lengths and it is possible that a wave length will be found which will prove lethal to some if not all malignant cell elements. Much work has been done along this line in the Cancer Research Laboratory of Sydney University by Moppett, work that is full of promise. We can only hope that success will crown his efforts and that the lethal wave length will be found before long.

Classification.

Classification is at best artificial and arbitrary. Recent research work goes to show that there is no real difference between innocent and malignant growths; they are both based on the same fundamental process of cell activity. The student of surgical literature will find that there is no more confusing subject than the classification of bladder tumours, particularly the epithelial bladder tumours. Perhaps that given by the late J. Geraghty, based on the original of Kuester and Albarran, is best from a descriptive point of view:

Benign—Simple papilloma, adenoma;

Malignant—malignant papilloma, papillary carcinoma, adeno-carcinoma, scirrhous carcinoma, squamous carcinoma.

Broders in 1921 put forward a classification from a new point of view. He classifies all malignant epithelial growths of the bladder from a survey of the cells as seen in a cross section by microscope. To use his own words: "A neoplasm can accomplish only what its cells can accomplish; if its cells are active, it is active. A neoplasm may be of papillary form and a low degree of malignancy or it may be papillary and a high degree of malignancy. Similarly, a sessile tumour accompanied by ulceration may be of a low or a high degree of malignancy."

He maintains that the grade of malignancy depends not so much on the general form of the growth, as on the proportion of differentiated cells resembling those of normal bladder epithelium, to the undifferentiated spherical and undifferentiated irregular cells with prominent nucleoli.

If 25% or less of the neoplasm is undifferentiated and 75% is differentiated, it is a malignancy of one degree. If the two groups of cells are equal, it is a malignancy of two degrees. If the undifferentiated cells form 75% and the differentiated 25%, it is a malignancy of three degrees. If all the cells are undifferentiated, it is a malignancy of four degrees.

The mortality rate of a large series of operations for bladder tumour was reviewed by Broders and it showed a wonderful parallel to his classification of the same tumours. In those that he classified as of one and two grades of malignancy, the results were uniformly good with very few exceptions. On the other hand, those that he classified as of three and four grades of malignancy yielded the highest rate of mortality.

Not so long ago we shared with others the belief that some epithelial bladder growths of the so-called villous, simple papillomatous type were benign, but repeated observations in many cases have forced us to the belief that all epithelial bladder tumours are malignant. If left alone, they will eventually kill the patient.

Ætiology.

There is nothing in our observations to suggest the cause of bladder tumours. The workers in the aniline chemical factories of Germany are said to have a high susceptibility to the disease.

Incidence.

In reviewing our cases we find that men are much more liable to bladder tumours than women in the proportion of about four to one. The disease never attacks infants. Children in their teens are also unaffected in our series, but some cases are recorded in surgical literature. In the twenties the incidence begins to show and every decade up to the sixties has an increasing number; from that time onward, the number declines. Our youngest patient was a man of twenty-two years, the oldest a man of eighty-four years.

Diagnosis.

Diagnosis is based on the history, but mainly on the cystoscopic examination of the patient. By far the greatest number of patients suffering from a bladder growth of the first two grades of malignancy, had a painless terminal hæmaturia as an initial sign of their disease. It is usually bright and quite frequently seen in the last few drops of urine. This was difficult to explain until on one occasion when a large papilloma was exposed through a wide suprapubic incision, it was noticed that part of the growth was caught within the circle of the vesical sphincter. It is not hard to imagine how during the act of micturition the floating delicate fronds of the vesical papilloma are caught in the swirl of the outgoing stream and swept through the outlet of the bladder. This can happen only when the stalk or pedicle of the growth is long enough to let one or more of the fronds reach the outlet. Once in the urethra, the voluntary and involuntary muscular efforts of the final act of micturition squeeze out blood from the growth. Not until the bladder fills with urine does the growth slip back into its former position. Confirmation of this explanation was found on more than one occasion, when on cystoscopic examination the distal end of a single papilloma was found bruised and blood stained, where it had been strangled in the grasp of the vesical sphincter.

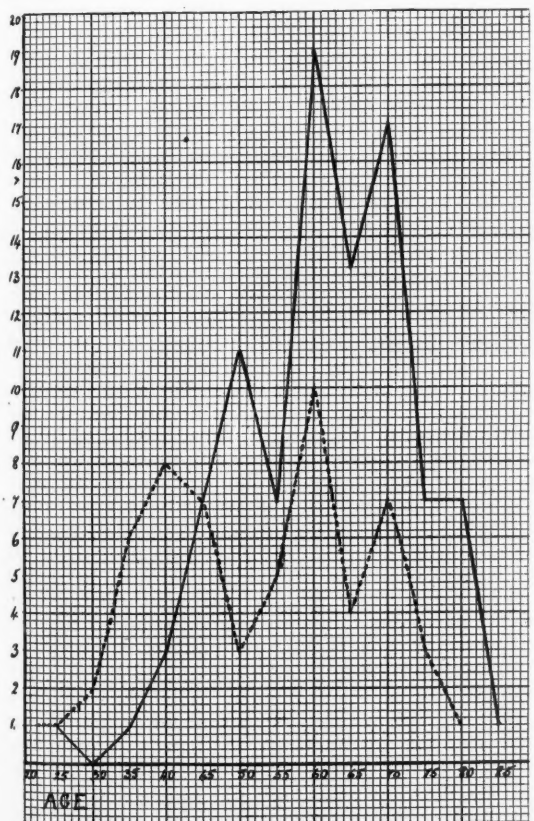

Figure I.

This explanation is true of some hæmaturias arising from papillomata of the first and second degree of malignancy, particularly those hæmaturias that appear at the very end of micturition; but it is not true of all. When the growth is advanced and large in size, the blood is squeezed from it by the contraction of the bladder, much as water is squeezed from a bath sponge by the hand. Accordingly the urine in these advanced cases is never free from blood.

On the other hand in cases of the third and fourth degree of malignancy, the tumour may be fairly far advanced before blood appears in the urine. Particularly is this the case when the new growth is on the inferior half of the bladder. An accompanying cystitis with pain and frequency of micturition is more often the symptom noticed by the patient. Smoky or dark blood-stained urine is usually thought to be of renal origin, but the bladder growth may bleed slowly and allow sufficient time for the chemical elements of the urine to act upon the red hæmoglobin and convert it into brown methæmoglobin.

In severe hæmaturia it may be difficult to determine by cystoscopy where the blood is coming from, but with the direct irrigating cystoscope of Braasch it is seldom that a view cannot be obtained sufficient to diagnose the presence, if not the extent of a growth. An examining finger in the rectum or vagina is of considerable help in determining the presence and extent of infiltration.

Those patients who consult a medical man at the very first sign of blood in their urine, are the exception; they usually wait until they get some pain. Even when the earliest advice is sought, the growth must already be of considerable size, sufficient at any rate to reach the vesical sphincter.

In reviewing our cases, we find that the general public is gradually learning the significance of blood-stained urine, especially when it is unaccompanied by pain. This, we feel sure, is the result of

a better understanding of bladder growths by the profession. Even a few years ago it was quite a common thing for patients to have months of treatment by drugs and prolonged rest. One patient was kept in bed or at rest for six months, as occasionally the blood would cease for a few days or sometimes for a week or two. When he was examined he was found to have an inoperable cancer involving the upper half of the bladder.

As a contrast to this, the last two patients referred to us were sent by their medical attendants on the day after the first appearance of blood in the urine. Both had a single papilloma amenable to treatment by diathermy through the cystoscope.

Operative Treatment.

It is depressing to note what a large number of patients suffering from cancer of the third and fourth degree of malignancy could not be given the hope even of an exploratory operation; also what a number, even when explored, could not be given a chance of a radical operation. This is true also of cancer in other parts of the body, such as cancer in the gastro-intestinal tract.

If cancer of the bladder of the first and second degree of malignancy is recognized early, surgery can hold out good hopes of a cure. But that cure is not complete when the operation is over. A definite system of repeated examinations must be made for a period extending over five years. One patient had a recurrence seven years after the original operation, although he was periodically examined and found free during a period of five years. Another patient with recurrent multiple papillomata has been kept alive for fourteen years. During that time she has had three open suprapubic operations with diathermic destruction of the growth, in addition to sixty treatments through the cystoscope for implantation recurrences. She is now freer from the disease than at any time throughout the whole period of treatment. During the prolonged period of treatment, this patient at one time went successfully through a pregnancy; while she was in the latter months of this event she could not, of course, be treated. When the pregnancy was over, the bladder was opened suprapubically to deal with the rapid advance of the disease. A pathological examination of the growth at this time showed that the character of the cell elements had altered. It was no longer a first grade malignancy; it was almost of the second grade. Since that time the menopause has occurred. Either due to this fact or to the closer watch and repeated treatment of all recurrences, the bladder is free from all growths except a small area near the suprapubic scar. Further, the pathological report of the last specimen shows that the recurrences are again reduced to the first grade of malignancy. From the progressive diminution in area and virulence of the growth it is probable that this patient will eventually be cured in the full sense of the word.[1] The fortitude, the patience, the intelligent and earnest cooperation of this patient have in no small way contributed towards this result.

When the bladder growth is small and of the papillomatous type irrespective of its degree of malignancy, the treatment can be carried out through the cystoscope. There is one exception to this rule and that is when in men the bladder growths are situated around the vesical neck. In women, even in this situation it is usually possible to destroy the growths, if a suitable cystoscope or urethroscope is chosen.

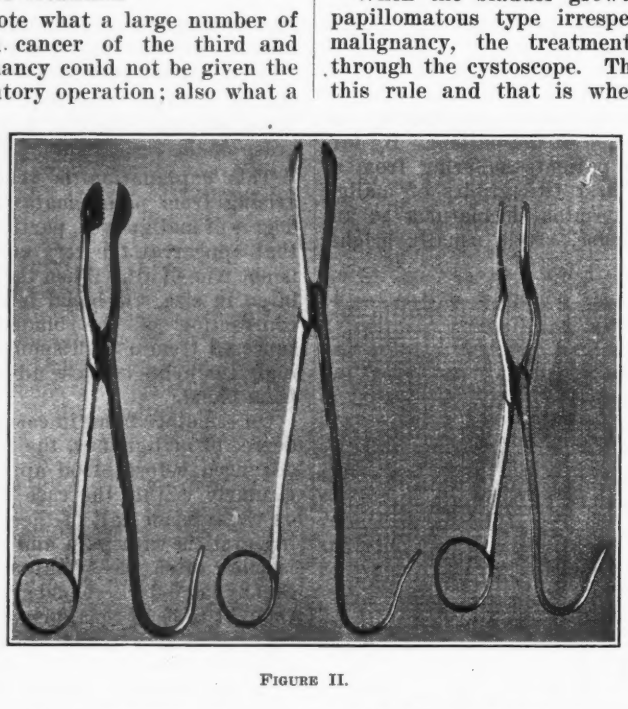

FIGURE II.

In advanced cases of multiple papillomatous growths or single large papillomatous growths open suprapubic operation is indicated with destruction of the growth or growths by powerful diathermic currents. The small portable apparatus is quite useless for this work.

The sessile growths of the third and fourth degree of malignancy, those that are like the iceberg much bigger underneath than on the surface, show such a poor response to surgical treatment by wide excision that we have almost abandoned this method. There is one axiom that must be kept in mind by workers in this surgical field. If the patient cannot be made better, at least he should not be made worse by the treatment used. Some of our earlier patients we not only failed to cure, but we made them worse. An implanted, fungating, stinking suprapubic growth was added to their sufferings. In a few dramatic relief has followed exposure with wide destruction of a phosphate-encrusted malignant ulcer, which was accompanied by unbearable cystitis. The ulcer healed and the cystitis disappeared. One old lady lived for two years after this treatment in perfect comfort. She

[1] Since this was written she has been free from all signs of recurrence for a period of three months.

died of postoperative pneumonia when a small painless local recurrence had been discovered by routine examination. One case only can we record of cure of a third degree malignant tumour of the vault of the bladder. He was a man sixty-five years of age, an engine driver. He is alive and at work five years and two months after the operation. He was treated by open operation and diathermy.

When it was necessary to open the bladder we used in our earliest cases to drain by a glass tube routinely, but during the last ten years we have reserved this procedure for those patients who have infected bladders. We are satisfied that immediate suture of the bladder wall at the time of operation is a safe procedure and shortens convalescence by one or two weeks. A rubber tissue drain in the form of a piece of rubber glove is always left in the space of Retzius for a few days.

Local anæsthesia we find is satisfactorily obtained by cocaine applied in a 20% solution on a wooden "applicator," in the same way as the oto-rhinologist applies it to the nasal septum. This urethral local anæsthesia is sufficient for those cases treated through the cystoscope. For severer types we find that sacral anæsthesia as used by Labat is eminently satisfactory. General anæsthesia is reserved for those patients who require open operation and a long and careful diathermic treatment.

Summary.

1. Up to the beginning of this century the results of surgical treatment of epithelial bladder growths were bad.

2. Epithelial bladder growths are all malignant and are divisible into four degrees of malignancy.

3. The results of diathermic treatment applied through the cystoscope to small papillomata of the first and second grade of malignancy are good.

4. Diathermy in the two severer grades of bladder growths shows better results than even wide excision.

5. The position of radium and X rays in the treatment of bladder growths has yet to be defined.

6. The better results of present day treatment are due to the fact that the profession and through them the public are recognizing the fact that blood in the urine unaccompanied by pain is very often the first sign of cancer of the bladder.

References.

(1) Thompson: "Diseases of the Urinary Organs," 1888, page 422.
(2) *Ibidem*, page 427.

DR. S. HARRY HARRIS (Sydney) stated that simple papillomata of the bladder were not definitely palpable in bimanual examination. Infiltrating palpable tumours were not amenable to diathermy and gave bad results even with the widest type of excision unless freely removed. Such growths though sometimes apparently cured by intravesical methods, had at an early date shown evidence of intravesical recurrence. The treatment of noninfiltrating papillomata, even if malignant, he considered a matter very largely of cystoscopic technique. In his experience these, even when large or multiple, almost without exception yielded to diathermy. His experience of X ray and radium treatment had been a very disappointing one.

MR. CAMPBELL BEGG (Wellington) drew the attention of members to an accident recently reported in the *Journal d'Urologie* in which an explosion occurred in the interior of the bladder during the progress of a fulguration. The current in use at the time was 600 milliampères. Until the actual cause of this was ascertained, it might be as well to refrain from using currents of high ampèrage in the closed bladder.

It was interesting to dwell upon the peculiar types of growth found in the bladder, the lower part of which was of mesothelial origin while the upper was endodermal. In both squamous epitheliomata considered typical of epiblast were found as well as adenomata of the intestinal type containing goblet cells.

The latter often took their origin in the lower end of the urachus which contrary to the usual teaching retained a very active epithelial core throughout life. The urachal cells which were derived from the ventral cloaca, were restless in their cramped environment and in a large percentage of apparently normal persons were found to have pushed their way into the stroma to form columns of cells which acquired lumina by central degeneration. These adenomata sometimes assumed malignant characteristics and broke into the bladder forming the well-known adenomata of the vault.

The practical application of this fact was that it indicated the free removal of the urachus and the surrounding tissues when a growth at the vault of the bladder was being resected.

MR. GORDON CRAIG replied that up to five years previously he had not used cystoscopy. The information obtained with the cysto-urethroscope enabled him to judge of the best type of operation to use. If there was difficulty in passing the instrument, he refrained. Any bleeding points, such as occurred at the prostatic bar, were arrested by a diathermy electrode. By doing this he had saved many a patient from a preliminary suprapubic cystotomy.

THE SURGICAL TREATMENT OF RAYNAUD'S DISEASE AND SIMILAR CONDITIONS.

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THE introduction of sympathetic ramisection has stimulated interest in the surgery of the peripheral blood vessels. In my first paper I have pointed out that vasodilatation followed the operation of sympathetic ramisection. These changes were at first acute, that is to say for some days there was a reddening of the skin and a feeling of warmth perceptible both to the observer and the patient. The acute changes gradually subsided, but even after an interval of three years the limb on the side from which the sympathetic nerves have been removed, is distinctly warmer than on the intact side. These facts have been rediscovered by certain American writers, notably Adson and Brown[1] and Kanavel and Davis,[2] who published papers on the treatment of Raynaud's disease and allied conditions. Previous to the introduction of ramisection, disturbances and diseases of the circulation due to vasoconstriction were treated by means of periarterial sympathectomy, popularized by Leriche. Although satisfactory results have been reported from this procedure, considerable doubt has been thrown on the anatomical basis of Leriche's operation by the researches of Kramer and Todd,[3] who showed that the sym-

pathetic nerves supplying the vasoconstrictors did not travel by means of the blood vessels, but were given off at irregular intervals from the segmental nerves. In his latest paper, however, Leriche[4] now adopts ramisection in cases of Raynaud's disease that resist periarterial sympathectomy. This means that practically the only line adopted in the treatment of Raynaud's disease and allied conditions is now by means of ramisection or by ganglionectomy of the sympathetic nervous system. We have then to consider only the most effective way of dealing with vasoconstriction.

Anatomy and Physiology of the Vasomotor Nerves.

It has been shown that there are two classes of vasomotor nerves, the vasoconstrictors and the vasodilators. As is the case of voluntary muscle and of the muscles of the bowel, these have two distinct nerve supplies. Vasoconstrictors are supplied by the sympathetic nervous system and the vasodilators are apparently supplied by nerves that travel along with the sensory nerves but in the opposite direction through the posterior nerve roots. These have been called by Bayliss antidromic fibres. The effect of cutting the sympathetic nerves is to cause a dilatation of the small arteries and arterioles, but after section of the vasoconstrictors a state of more or less contraction still exists which can be still further reduced by stimulation of the antidromic nerves. According to Bayliss this moderate tone left by section of the constrictors increases in a few days and becomes nearly equal to the original tone in some weeks. In clinical experience the removal of the vasoconstrictors leads to an immediate vasodilatation of the peripheral vessels. Adson and Brown have shown that the evidence of increased blood flow persisted for at least six weeks in five cases of spastic paraplegia in which lumbar sympathetic neurectomy had been performed for spasticity. They also observed that the skin temperature increased from two to seven degrees following operation. An increase in heat production and radiation from the feet from 200% to 900% was also noted.

I have observed vasomotor changes as evidenced by increased temperature in the lower limb after a period as long as three years.

Raynaud's disease is caused through the abnormal sensitiveness of the vasoconstrictor nerves resulting in a continuous or intermittent spasm of the smaller arteries and arterioles of the extremities. It may be due simply to exposure to cold or it may be dependent upon toxic or psychic influences. The colour changes observed in Raynaud's disease are dependent upon arterial constrictures. The whiteness of syncope indicates a complete closure of the arteries, while the asphyxia which supervenes after a time, is due to the difficulty of the blood in passing the small capillaries or to less complete closure. According to Adson and Brown the capillaries become more dilated during the periods of asphyxia with stasis of blood and the blood becomes blue. They observed complete capillary stasis over a period of thirty minutes.

The Anatomy of the Vasomotor Nerve Supply.

The vasoconstrictors are more or less the continually acting principle of the nerve supply and are dependent upon the sympathetic nervous system just as posture in the bowel is also dependent upon the same nerve supply. These sympathetic nerve supplies are derived from the thoraco-lumbar outflow and reach the ordinary segmental nerves by means of the grey *rami communicantes*. It is, therefore, evident that to relieve vasoconstriction of the peripheral blood vessels and to produce a maximum effect it is necessary to divide the *rami communicantes* at their source.

The Anatomical Basis of the Operative Treatment.

It is quite clear that there is no necessity to remove the whole of the abdominal sympathetic trunk as practised by Adson and by Kanavel and Davis. The effect produced in my patients suffering from chronic constipation and retention of urine by the division of medially directed *rami* supplying the bowel indicates that the complete removal of the abdominal sympathetic could have an undesired effect on the viscera. The effect upon the upper limb can be obtained by cutting the *rami communicantes* as they enter the nerves of the brachial plexus and there is no necessity to remove the whole cervical sympathetic trunk. In their early cases Davis and Kanavel removed the entire sympathetic trunk, but suggest a modification by removing the superior thoracic and inferior cervical sympathetic ganglia, their branches and the intervening trunk. They say, in addition, that it is quite unnecessary to remove the superior and middle cervical ganglia, as by this means they added the symptoms of Horner's syndrome unwarrantedly. How they avoid this syndrome in their operation of removal of the superior thoracic and inferior cervical ganglia and of the intervening trunk is not explained. In addition to removal of the abdominal sympathetic trunk, Adson and Brown carry out a periarterial sympathetic neurectomy of the common iliac arteries. The necessity for this latter procedure is not clear, since the whole effect described by them can be obtainedby simply dividing the abdominal sympathetic trunk below the third lumbar nerve. This is a very much less mutilating operation and preserves intact the sympathetic supply to parts not usually affected in Raynaud's disease.

If it is desired to affect the whole blood supply to a lower limb, the laterally directed *rami* to the second and third lumbar nerves should be divided in addition to division of the trunk below the third lumbar nerve. In the cervical region an ordinary ramisection, that is division of the *rami communicantes* as they enter the nerve roots, makes a satisfactory operation. A division of the *rami* as they leave the superior thoracic ganglion, is open to the objection that some of the upper roots of the brachial plexus receive fibres directly from the cervical sympathetic trunk.

The Effect of Ramisection upon Healing.

It is interesting to note the effect of ramisection upon healing in the laboratory animal. Immediately

after the operation of ramisection the wound is filled with serum and healing is not as rapid as on the unoperated side. In a few days, however, the picture is altered with the loss of the acute vasomotor changes. The wound on the side from which the sympathetic nerves have been removed, then heals a little more rapidly than on the normal side.

There are eight cases in the series that I present. Four of these were diagnosed as *thrombo-angiitis obliterans;* the other four were cases of typical Raynaud's disease. In *thrombo-angiitis* the result is at first satisfactory, but as the acute hyperæmia wears off, there is often a return of pain, though the circulation of the limb is in a much more satisfactory condition than before operation. In Raynaud's disease the results are much more successful and permanent. In all cases except in one the disease affected the lower limb and the operation led to a complete relief of symptoms. In the one case in which the upper limbs were subjected to operation, the result was not as complete, though in the lower limbs of the same patient the result was satisfactory. The patient had had Raynaud's disease for about fourteen years and it is probable that there were actual structural changes in the blood vessels to account for the less satisfactory result.[1]

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(2) Loyal Davis and Allen B. Kanavel: "Sympathetectomy in Raynaud's Disease, Erythromelalgia and other Vascular Diseases of the Extremities," *Surgery, Gynecology and Obstetrics*, June, 1926, page 729.

(3) J. G. Kramer and T. Wingate Todd: "Distribution of Nerves to the Arteries of the Arm," *The Anatomical Record*, 1914, page 243.

(4) R. Leriche: (Fourteen Cases of Section of the Rami Communicantes arising from the Stellate Ganglion), *Bulletin et Memoires de la Société Nationale de Chirurgie*, 1915, *Volume* li, *page* 990.

Mr. Gordon Craig (Sydney) asked Mr. Royle if he had had the opportunity for doing a ramisection on a patient with *endarteritis obliterans* which was usually of syphilitic origin. He referred to the condition of a limb after Syme's amputation had been carried out for gangrene due to this condition.

Dr. Royle's answer was that if it were done early then it would be satisfactory.

Section IV.—Pathology and Bacteriology.

THE VALUE OF COMPARATIVE PATHOLOGY IN THE PROBLEMS OF HUMAN DISEASE.

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Over a period of many years medicine has been split into fractions and of recent years these fractions have become more and more separate and distinct from one another. Happily, some have fought against this and tried to bring some of the fractions into closer unity, to bring about "the unity of medicine as a biological study." The study of medicine has become so vast that no man can make himself a master of the whole, but in the intensive study of one branch or fraction we have forgotten the purpose of our study and we have failed to listen to and benefit by the discoveries and teachings of other branches or fractions. It is necessary that we should have some general view and conception of the whole and as great a coordination of the parts as possible.

As one whose early training was in the diseases of animals and whose later work has been mainly with the diseases of man, I take the liberty of bringing before your notice a point of view of which many, I feel, have failed to realize the value to science and human affairs generally. I wish to advance a plea for the comparative method and while this should be fully extended to the study of disease in man, animals and plants, my main concern will be an attempt to convince you that veterinary research has a great significance to science generally and to medical research in particular.

The study of disease has become and must remain highly specialized in its different branches, but advances in animal pathology have in the past interacted on and will continue in the future to interact on and to influence human pathology. Although Pasteur worked largely on the problems of the cause and prevention of diseases in animals, he was enabled to make such profound advances because he realized the unity of medicine as a biological study and the results of his studies bear on the problems of human disease as on other biological problems.

When Theobald Smith in 1893 communicated the results of his studies on Texas cattle fever to the Association of Physicians in Washington, little notice appears to have been taken of his epoch-making discovery of a pathogenic microorganism which could be transmitted only through the agency of an intermediary host. Later, malaria and other human diseases were found to be transmitted by a similar agency, but this method was first demonstrated in a disease of animals and the significance of it was not appreciated by the majority of physicians.

Many great men of the past have realized the value of comparative pathology and an outstanding name is that of John Hunter. More recently we find Sir William Osler closely associated with veterinary medicine and particularly interested in comparative parasitology and comparative pathology. It was largely due to the influence of Sir Clifford Allbutt and his interest in comparative pathology that the Royal Society of Medicine established a Section of Comparative Medicine in October, 1923. We are given the lead by very great men and we should attempt to follow. There appears to be no doubt that an attempt is being made in England and the University of Cambridge has recently established a chair for the study of diseases in animals.

[1] Details of cases were then given.

There has been a quickening of the interest in diseases due to those minute microorganisms generally classed as filterable viruses and in order to gain more information as to their nature and behaviour it has been necessary to study those associated with diseases in the lower animals. No doubt very important discoveries will be made in this field which will have bearings on the problems of human disease as well as disease in animals and plants. One of the viruses that has been most closely studied is that causing pleuro-pneumonia in cattle. It can be cultivated on artificial media with comparative ease and it has been shown by Heslop quite recently in work done at the Melbourne University Veterinary School that there are at least two types of this virus present in Victoria as determined by serological methods. This is the first time it has been demonstrated that a filterable virus may be divided into distinct types and the discovery is a very significant one.

In Australia and New Zealand the sheep and wool industries are of great economic importance but little work has been done on the diseases of sheep. Apart from the economic importance of the diseases of sheep the study of them offers unusual difficulties and the solving of many of the problems associated with them may throw new light on the pathology of many of the diseases of man and the lower animals. Pregnant ewes are subject to toxæmias of pregnancy which resemble in many respects those found in the human subject. In some types the mortality is very high and we find the same necrosis of the liver that is observed in the human subject. A systematic investigation of this disease is very necessary. One remarkable feature is that the disease becomes manifest in a flock in certain years, although it may be absent in other years and when it does appear, the number of animals attacked may be considerable. This probably indicates that external factors play a large part in the production of the disease and if these can be determined and the mechanism explained by which the symptoms of the disease are produced, great assistance may be given to the study of the disease in the human subject. I have examined the urine from some sheep with this disease and have found that the urea-nitrogen is lowered and the ammonia-nitrogen is raised as in eclampsia in the human subject. The proportion of ammonia-nitrogen to urea-nitrogen has been found to vary in normal sheep from 1:137 to 1:67, while in sheep showing symptoms of toxæmia of pregnancy the results have been found from 1:33 to 1:9. Acetone and diacetic acid have also been found in large amounts. A systematic investigation of this disease is almost sure to throw considerable light on the nature and cause of the toxæmias of pregnancy in man and the lower animals. The opportunities are great as plenty of material is available with little or no limit on experimentation.

In the same category is that interesting disease of dairy cows known as "milk fever." This disease occurs at the termination of parturition and is manifested by loss of appetite, restlessness and sudden loss of consciousness, with sometimes spasms in groups of muscles. The ætiology of the disease has remained quite obscure, but in spite of this, treatment by inflation of the udder with air has proved very successful. Little and Wright have recently demonstrated that the calcium content of the blood-plasma of cows suffering from milk fever shows a considerable fall, from 20% to 30% in mild to 60% in severe cases. Widmark and Carlens have shown that the blood sugar of milking cows falls to 0·040% from 0·085% which is the normal value for cows not in milk. Following the administration of "Insulin" symptoms identical with milk fever develope. They further showed that the injection of air into the udder of cows causes a prompt rise in blood sugar in lactating animals. This is probably due to the sudden interference with the functioning of the cells of the gland causing glucose to accumulate in the blood. They did not extend their observation to actual cases of milk fever. Confirmatory evidence of a hypoglycæmia in milk fever is lacking at present and Little and Wright have reported that the blood sugar may be higher when the animal is comatose than when recovered. It seemed rather too good to be true that milk fever was really a hypoglycæmia due to exhaustion of the blood of its sugar and that inflation of the udder allowed the glucose level in the blood to become readjusted. The results of Little and Wright show, however, that there is a decided fall in blood calcium and if anything a tendency towards a higher blood sugar value than normal. As there is an increase in the phosphorus-calcium ratio in the blood in eclampsia and a definite tendency towards a hyperglycæmia according to the work of Stander, it seems possible that milk fever and eclampsia are closely related conditions. A closer study of milk fever in bovines should prove of value in helping to elucidate the problems associated with the toxæmias of pregnancy.

There are many other diseases of sheep which are of interest to the comparative pathologist. Lambs are subject to dysentery which does not appear to be caused by an obligate parasite and *Bacillus welchii* has been incriminated. Recent experimental work by Dalling appears to strengthen the case against this bacillus. Lambs are also subject to a fulminating type of intoxication with sudden death. About the time these diseases make their appearance the lambs are changing from a diet rich in animal protein to a vegetable diet and the bacterial flora of the intestinal canal would almost certainly become modified in consequence. It is possible that a study of these diseases would throw light on the change in the intestinal flora associated with change in diet and the mechanism of gastro-intestinal disturbances in young animals.

Osteo-arthritis is known to occur in sheep and other animals and the elucidation of the conditions, associated with the production of lesions of this nature in animals may help in the study of similar problems in man.

Of recent years botulism has become more common particularly in America where home-canning of

fruit and vegetables is a common practice. Botulism is not uncommon in animals, particularly in horses and cows and in Australia the condition has been studied particularly by Seddon and myself. Although the disease had been known in horses for some years in Australia, it was not until 1921 that I was able to obtain on two separate occasions evidence of the presence of an anaerobic bacillus of the botulinus group in some damaged wheat grain that was suspected of being associated with the death of horses. No serum was available at that time for typing purposes and attempts to isolate the toxin-former failed. In 1922 Seddon published the results of a bacteriological examination of a bacillus of this group isolated from the bones of a cow which had been dead for some months. He called the bacillus *Bacillus parabotulinus* and later it was found to be the same as or a subgroup of *Bacillus botulinus* type *C* which had been isolated in America by Bengtson from the larvæ of *Lucilia cæsar*.

Since that time I have examined chaff, mouldy meadow hay, cocky chaff, oats, damaged wheat grain, hay, mouse fæces from hay and bones from a carcase of a horse on ten separate occasions making twelve in all and have obtained evidence of the presence of *Bacillus botulinus* type *C* on three occasions. It is probable that it was the same bacillus in the two previous toxic cultures from damaged grain and if this is so, then I have obtained five positive results in twelve examinations. The positive results were obtained from wheaten chaff, oat seed and cocky chaff once each and twice from damaged wheat grains lying on the ground after winnowing operations. Seddon has obtained the same organism from the bones of a sheep and those of an ox.

Up till quite recently neither *Bacillus botulinus* type *A* nor type *B* had been discovered in Australia, but in 1925 Seddon recorded the finding of type *B* in maize ensilage the feeding of which had led to the death of three cows and three horses after they had manifested the symptoms of botulism.

In 1924 I obtained a bacillus of the botulinus group from a sample of surface soil taken from a farm on which horses had died from botulism and *Bacillus botulinus* type *C* discovered in the cocky chaff on which the animals had been fed. This bacillus from the soil is apparently yet another type of *Bacillus botulinus* as the antitoxins of *A*, *B* and *C* do not protect against its toxin.

The spores of *Bacillus botulinus* type *C* and of this bacillus from the soil are not very resistant to heat which incidentally makes the isolation of these bacilli a difficult matter. The spores of types *A* and *B* are very resistant to heat and on this account they are often responsible for the toxic spoilage of foods subjected to certain degrees of heat for preservation purposes.

The results of these investigations in Australia which were primarily concerned with the elucidation of problems of disease in animals, are nevertheless of interest and some importance to physicians in human medicine. In the first place, they have demonstrated that *Bacillus botulinus* type *C* is the common type of the group in Australia. Should cases of botulism occur in the human subject in Australia, it is reasonable to expect that type *C* might be responsible. If type *C* were responsible, it would be useless to employ any other than type *C* antitoxin for treatment or prophylaxis. There is another point, however, which brings even greater satisfaction than the first and this is that as the spores of type *C* are not very resistant to heat, there is considerably less danger of their not being destroyed during the heating processes adopted in canning foods. Were types *A* and *B* more common in Australia, our position would be less secure.

No attempt has been made to make a survey of the field and indicate in what measure the study of the diseases of animals has helped in the problems of human disease and from where the greatest help can be expected to come in the future. I have attempted to show in a general way that the study of animal diseases is of value to science generally and in particular to medical research and I have relied mainly on my own small experiences, wheras the case could have been made a hundredfold stronger if I had shown you what had been accomplished in the past by many brilliant workers. Of course the results are not always of great or immediate practical value, but they add to knowledge and sometimes unexpectedly lead to knowledge of very great practical value. One may go as far as to say that every accurate observation on a pathological process in an animal is of value in the study of human disease.

As an illustration of the truth of this statement may I be permitted to mention one instance out of my own experience? For some years I had been interested in a type of granuloma of horses situated commonly on the conjunctiva, the urethral mucosa at the orifice and on the skin. This granuloma has very distinctive characteristics both macroscopic and microscopic. In the early examples which I studied, I was unable to determine the cause of the condition, but later younger specimens were examined and it was found to be due to the granulomatous reaction around small larval nematodes. This nematode was found to belong to the genus *Habronema*, three species of which live as adults in the stomach of the horse. Ransom had worked out the life history of one of these species, but that of the other species was determined by Hill and myself independently. I was able to produce the granuloma under experimental conditions by larvæ bred artificially in flies. On account of this study I acquired some knowledge of the reaction of the tissues of the body to the invasion of these larval worms. In 1922 I had submitted to me a small tumour from the conjunctiva of a child for microscopic examination. This revealed the characteristic microscopic picture of a granuloma due to a larval *Habronema*. It was probably produced by larvæ escaping from the proboscis of a fly which had come to suck moisture from the conjunctiva of the child. The larvæ had burrowed beneath the epithelium of the conjunctiva where they had irritated the tissues and come to their death. Since that time I have seen one other

granuloma of this type from the same situation in the human subject. Without previous experience I would not have been able to recognize the true nature of the tumour. This type of granuloma has not been described as occurring in the human subject elsewhere. Is it reasonable to conclude that it does not occur anywhere else in Australia or other parts of the world? As the genus *Habronema* is common in all parts of the world and as the larvæ are to be found in species of muscid flies, it is more reasonable to conclude that this type of granuloma may be found occasionally in any part where horses are kept, but that it has remained unrecognized. The point I wish to make is that the more complete our knowledge is, the less frequent will be our failures to recognize the true nature of disease processes and that we should use every source in order that our knowledge may be the more complete. The study of comparative pathology should be recognized as a very fruitful source of knowledge of disease processes and there should be a greater effort made in this study for its own value and a closer unity between those so engaged and others concerned in the problems of human disease.

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DR. W. GILMOUR (Auckland) said that he had had no great experience in work with animals. He knew of one case of botulism in New Zealand, the source apparently being from a tin of peaches obtained in Australia. He had examined other tins of peaches from a similar source and had found that they were all in good order.

DR. C. S. M. HOPKIRK (Dunedin) said that there were one or two points raised by Dr. Bull concerning which he did not agree with him. In regard to filterable viruses Dr. Bull said that there were only two distinct types in pleuro-pneumonia. He said that there were two or more types in foot and mouth disease. Dr. Bull had described one case of toxæmia of pregnancy in one flock. In New Zealand it was found frequently and only in sheep on high-class pasture. By giving the sheep exercise the disease was overcome. Milk fever was overcome by the injection of air into the udder. He found that by injecting glucose intravenously a cure was also obtained and hence he thought that milk fever must have some association with hypoglycæmia. Vaccines were being used successfully in the treatment of dysentery in lambs. Osteoarthritis was not found in adult sheep in New Zealand, but was common in lambs. It was due to *Bacillus pyogenes*. Botulism was not common in New Zealand, but there had been a suspicious outbreak in Christchurch. Parabotulism was unknown. Epithelioma of the nictitating membrane in horses was unknown in New Zealand, but a similar condition was seen in cattle. Many cows, sometimes 50% of a herd, in New Zealand had difficulty in becoming pregnant. He felt sure that this was due to some inflammation of the cervix. Associated with this condition a cystic *corpus luteum* was found. There was some connexion other than bacterial between this and the cervicitis.

DR. P. P. LYNCH (Dunedin) said that there was much arthritis in lambs in New Zealand. He had found *Staphylococcus aureus* in cases of arthritis and he thought that possibly it was a metastatic infection from tailing.

PROFESSOR J. B. CLELAND replied on behalf of Dr. Bull that as far as he knew there were no recorded cases of botulism in Australia. Before lethargic encephalitis had been recognized, there had been obscure cases of diplopia in Australia. These might have been encephalitis or perhaps botulism. The arthritis of lambs to which he referred, was a quite definite condition with no evidence of any preceding pyogenic infection. The pathology was similar to that of arthritis in man. With reference to the cystic *corpus luteum* he had seen a short time ago a cow after abortion in which there were symptoms resembling tetanus. At the *post mortem* examination it was found that abortion had occurred and there was also a cystic *corpus luteum*. It was suggested that this was responsible for abortion taking place. This showed the importance of veterinary pathology in relation to human disease.

A COMPARATIVE STUDY OF THE KAHN AND WASSERMANN TESTS IN 6,000 CASES.

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DURING the last few years many papers have appeared in the literature in which the correlation between the complement fixation test for syphilis and the flocculation test devised by R. L. Kahn are discussed.

During the last three years we have performed a Kahn as well as a Wassermann test on each specimen of serum submitted to this laboratory for the latter purpose. In the present paper the comparative results obtained in the last six thousand cases are briefly reported.

The details followed in setting up the Kahn test are those described by Kahn in his recent book.(1)

For the Wassermann test we have followed with certain modifications the technique of Griffiths and Scott.[2] The modifications which we employ are two in number.

Firstly, we use Kolmer's new cholesterolized and lecithinized antigen in place of the antigen used by Griffiths and Scott. Secondly we perform a quantitative test with every reacting serum, by varying the dilution of the serum according to Kolmer's quantitative technique.

The specimens of serum which form the basis of the present report, have been forwarded for examination from the Dunedin Public Hospital, the Seacliff Mental Hospital and the Dunedin Venereal Diseases Clinic and from private practitioners and smaller hospitals. The majority are from the Dunedin Hospital, where blood is collected as a routine from the majority of patients admitted.

For the purpose of this report the patients from whom serum has been examined may be divided into two groups: Those patients whose serum is being examined for the first time either as a routine or because of suspected syphilis; those patients who have been diagnosed as syphilitics and who are at various stages of antisyphilitic treatment.

The results in the first group are summarized in Table I. From this table it will be seen that of 5,369 specimens of serum of untreated patients examined there was complete agreement between the results of the Kahn and Wassermann tests in 5,309 or approximately 98·9%. In the remaining sixty specimens in this group results of the two tests did not coincide. The disagreements will be considered in the order in which they appear in Table I.

TABLE I.—UNTREATED PATIENTS.

Agreement Between the Results of the Two Tests.

Response to the Tests.		Number of Patients.
Kahn Test.	Wassermann Test.	
No reaction	No reaction	4,892
Reaction	Reaction	417
		5,369

Disagreements Between the Results of the Two Tests.

Response to the Tests.		Number of Patients.
Kahn Test.	Wassermann Test.	
Reaction	No reaction	3
Reaction	No reaction	29
No reaction	Reaction	4
Reaction	Anticomplementary	7
No reaction	Anticomplementary	6
Doubtful	Reaction	5
Doubtful	No reaction	6
		60

Total number of patients examined	5,429
Percentage of absolute agreement..	98·9

(i) The serum reacts to the Kahn test but not to the Wassermann test (known syphilitics).

Of the three patients in this group the condition in two was diagnosed as primary syphilis and in one as congenital syphilis.

(ii) The serum reacts to the Kahn test but not to the Wassermann test (false Kahn reactions).

The results in twenty-nine instances in this group may be attributed to false Kahn reactions. A further specimen of serum was obtained from each of twenty-three of the patients and on examination twenty of the twenty-three failed to react to the Kahn test. There was nothing to justify a diagnosis of syphilis in the remainder.

(iii) The serum fails to react to the Kahn test but does so to the Wassermann test.

Of the four patients in this group the conditions of two were diagnosed as tertiary and two as cerebro-spinal syphilis. The absence of a reaction to the Kahn test may therefore be regarded as a false failure.

(iv) The serum reacts to the Kahn test and yields an anticomplementary Wassermann reaction.

The seven patients in this group were all definite syphilitics. The serum of two was persistently anticomplementary after repeated examinations of further specimens. The serum of the remaining five gave definite reactions on examination of further specimens.

(v) The serum fails to react to the Kahn test and yields an anticomplementary Wassermann reaction.

The serum of the six patients in this group did not react to the Wassermann test on re-examination. A number of anticomplementary results due to gross infection or hæmolysis have not been included in this series. The majority of the specimens was unfit for use in the precipitation test, owing to the presence of suspended particles from which they could not be rendered free.

(vi) The serum yields a doubtful reaction to the Kahn and a positive reaction to the Wassermann test.

Of the five specimens of serum in this group all were from persons with clinical evidence of infection. During several re-examinations after the institution of treatment a reaction to the Kahn test was obtained at some time in each case.

(vii) The serum yields a doubtful reaction to the Kahn test but no reaction to the Wassermann test.

In none of the six patients in this group could any evidence of syphilitic infection be found. On examination of a further specimen of serum from each patient no reaction to the Kahn test was obtained.

The results of group (ii) are summarized in Table II. From this table it will be seen that of 631 specimens of serum examined from patients with syphilis under treatment the results of the Kahn and Wassermann tests were in complete agreement in 541 or approximately 85·7%. The disagreements between the two tests in this series numbered ninety. The serum lost the power to react to the Kahn test, while it still yielded a reaction or weak reaction to the Wassermann test in forty-one instances. On the othe rhand,

the loss of power to react to the Wassermann test first occurred in only twenty-nine instances. In the serum of the remaining twenty patients there

TABLE II.—PATIENTS UNDER TREATMENT.

Absolute Agreement Between the Results of the Two Tests.

Response to the Tests.		Number of Patients.
Kahn Test.	Wassermann Test.	
Reaction	Reaction	370
No reaction	No reaction	159
Doubtful	Doubtful	12
		541

Relative Agreement between the Results of the Two Tests.

Response to the Tests.		Number of Patients.
Kahn Test.	Wassermann Test.	
Reaction	Doubtful	14
Doubtful	Reaction	6
		20

Disagreement Between the Results of the Two Tests.

Response to the Tests.		Number of Patients.
Kahn Test.	Wassermann Test.	
No reaction	Reaction	26
No reaction	Doubtful	15
Reaction	No reaction	14
Doubtful	No reaction	15
		70

Total number of patients examined	631
Percentage of absolute agreement	85·7
Percentage of relative agreement	88·9

was a relative agreement between the two tests, the difference being only one of degree of positivity. If we except these from the total of disagreements, the number of relative agreements in group (ii) becomes 561, out of a total of 631 tests or in other words approximately 88·9%.

Discussion.

The main advantages of the Kahn test as compared with the complement fixation test are its simplicity and economy. The only reagents required are antigen, serum and saline solution.

Nevertheless, the antigen requires as much care in its preparation and titration as does the antigen of the Wassermann test.

The chief disadvantage of the Kahn test is that the results are occasionally difficult to read and still more difficult to interpret.

As regards the specificity of the Kahn reaction, it would appear from our results that it is more likely to give falsely positive reactions than is the complement fixation test. In the present series we have no recorded case of a falsely positive Wassermann reaction, whereas we have a total of twenty-nine cases in which presumably the Kahn test yielded a falsely positive reaction. We have not included in the above series our results obtained with the serum of eighty patients with frambœsia (yaws), whose serum yielded both reactions equally strongly in every case.

Our records include only five patients with primary syphilis. The serum of two of these gave a reaction to the Kahn test at an earlier stage of the disease than to the Wassermann test. In the remaining three a reaction to both tests was obtained at about the same time.

It will be noted that our series includes thirteen patients whose serum was anticomplementary in the Wassermann test. In such cases as these where the serum is neither grossly infected nor much hæmolysed the Kahn test is of considerable value, as one is able to give a tentative report pending the receipt of a further specimen of serum for re-examination.

It occasionally happens that a patient is met with whose serum is persistently anticomplementary. The serum of two of our patients exhibited this phenomenon. In both the Kahn test yielded a strongly positive reaction. The condition of both patients diagnosed clinically as cerebro-spinal syphilis.

Doubtful or weakly positive responses to the Kahn test occur with greater frequency with the serum of patients that does not react to the Wassermann test or with the reacting serum of untreated patients than do similar responses to the complement fixation test.

Our experience with ice-box fixation overnight as employed in the Griffiths and Scott technique led us to conclude that in untreated syphilis a doubtful Wassermann reaction is of rare occurrence. This is not so with the Kahn test. Of the 436 examinations of the serum of untreated syphilitic patients included in the present series five gave a doubtful response to the Kahn test. The serum of six of the non-syphilitic patients gave doubtful results to the Kahn test. It is these doubtful results which are so difficult to interpret.

On comparing the results obtained in our patients under treatment it will be seen that power to react to the Kahn test disappeared before the power to react to the Wassermann test in forty-one cases and that the power to react to the Wassermann test disappeared before that to the Kahn test in twenty-nine cases.

In the Dunedin Venereal Diseases Clinic the practice has been to regard the persistence of a positive reaction with one test, after the response to the other has disappeared, as an indication for further treatment. Most of the discrepancies in the responses are of degree of positivity, so that the percentage of the comparative agreement between the two tests is very high, approximating 88·9%.

Over our whole series of six thousand patients the percentage of absolute agreement is 97·5%.

It will be readily seen that in comparing the results between the two in any series of cases the percentage of absolute agreement will vary with the number of patients under treatment included. The greater the number of treated patients included, the

lower will be the percentage of absolute agreement. Practically one-ninth of our series are under treatment.

Summary.

The inference to be drawn from the preceding comparative results may be summarized by saying that the Kahn test constitutes a reliable control to the complement fixation test. Of the two tests that of complement fixation still remains the more valuable, but to obtain the best results both should be employed.

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(2) Reports of Public Health Subjects, No. 1.

DR. A. B. PEARSON (Christchurch) said that he had had no experience of the Kahn test. He would have to adopt such a test because of its rapidity and simple technique. He thought it essential for routine work in a large hospital. With such a test one would be able to report on a blood specimen immediately without waiting to do a Wassermann test.

DR. W. GILMOUR (Auckland) said that he entirely agreed with Dr. D'Ath's work. He had tested one thousand patients by Kahn's method and had obtained 98% agreement with the result of the Wassermann test. He said it was easy to carry out, but at present its chief value was as a check to the result of the Wassermann test. In one or two cases of primary sore he had noticed the same facts as Dr. D'Ath. The reaction to the Kahn test appeared sooner and remained longer than that to the Wassermann test. All his results with the Kahn test were similar to those obtained by Dr. D'Ath.

DR. P. P. LYNCH (Dunedin) said that his results with the Kahn test coincided with those of Dr. D'Ath. He had carried out 3,400 tests; he applied the Kahn test one day and the Wassermann test the next day and compared the results. He got some disagreement. In treated patients it was more difficult to get agreement. In cases of primary sore the reaction to the Kahn test appeared sooner than did the Wassermann reaction. Patients under treatment reacted to the Kahn test for a longer period than to the Wassermann test. Taking the whole series of cases he obtained 95% agreement. He said that the Kahn test would not displace the Wassermann as a sole test, but it afforded a valuable check in alleged infections detected during the routine Wassermann examination. It helped the pathologist to give a diagnosis more confidently.

DR. G. PINESS (Los Angeles) said that he had been doing Kahn tests in his laboratory for some time to check the results of the routine Wassermann tests. His findings were similar to those of Dr. D'Ath's. At times he had noticed a precipitate in the second tube, although Kahn had stated that this should not occur. Others also had reported this finding of the precipitate. The Kahn test would never replace the Wassermann test, but it might be possible to find a better antigen or a new technique and so make the test more reliable.

DR. A. H. TEBBUTT (Sydney) said that in doing the Kahn test he had also had trouble with anticomplementary serum. He had thought that this was due to increased cholesterol, but later proved that this was incorrect. The anticomplementary qualities of serum increased on keeping. He found also that sometimes it was only a temporary quality of the serum. Anticomplementary serum was commoner among samples of serum yielding Wassermann reactions than among those that did not. It was interesting to note that Dr. D'Ath found that the response to the Kahn test in treated patients disappeared before the reaction to the Wassermann test, while Dr. Pearson and Dr. Lynch found the opposite. He agreed that the reaction to the Kahn test appeared earlier than that to the Wassermann test. He was very interested to hear that Dr. D'Ath did not obtain a single false Wassermann reaction.

Dr. D'Ath replied that his experience with anticomplementary serum was similar to that of Dr. Tebbutt. On keeping serum it sometimes became anticomplementary, while some anticomplementary sera prevented the reaction after storage. He had also noticed a precipitate in the second tube at times and this was one of the causes of doubtful reaction.

THE MORBID ANATOMY OF THE THYREOID GLAND IN HYPOTHYREOIDISM AND MYXŒDEMA.

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(*See August* 20, 1927, *page* 54.)

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TUMOURS OF THE THYREOID GLAND.

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SIMPLE TUMOURS.

Simple connective tissue tumours appear to be rare. In our material we have not met with any undoubted examples. Simple or benign epithelial tumours (adenomata), however, are not uncommon in New South Wales and present interesting and difficult features to the clinician, the morbid histologist and the student of new growths. At certain periods of life the thyreoid gland is subject to considerable variations in size, weight and microscopical structure (Eugenia Cooper[1]). These physiological cycles, hypertrophy and involution, are also met with in other organs, particularly in the female breast and the uterus and it is just in these organs and in the thyreoid that benign encapsulated

tumours are not infrequently met with. Few will question the classification of fibro-adenomata of the breast or fibro-myomata of the uterus, but there is some indecision in the literature on the subject of adenomata of the thyreoid. Applied to all benign encapsulated nodules the term will certainly connote a greater variety of histological structure than is found in the above-mentioned tumours of the breast or uterus, so that we have several different types of adenomata or those presenting several types of structure. We admit at once the difficulty of differentiating neoplasia from hyperplasia. A hard and fast frontier would be artificial in the present state of our knowledge. But the fibro-myoma of the uterus is not very dissimilar to the uterine muscle in which it lies, so that even if the thyreoid tumour appear to be comprised of relatively normal elements, it is not inconsistent or without precedent to use the term adenoma.

Any reference to this subject would be incomplete without allusion to the work of Marine.[2] He defined these benign tumours as circumscribed, localized and encapsulated growths of glandular tissue which retain more or less of the anatomical characteristics of the parent tissue. He considered that the development of these benign tumours is constantly associated with hyperplasia of the gland as a whole. His well-known anatomical and physiological cycle in diffuse enlargements, namely, normal thyreoid, hypertrophy, hyperplasia, atrophy or involution to colloid state and so on becomes in the nodular enlargements (adenomata), adenoma *Anlage*, hypertrophy, hyperplasia, atrophy or destructive metamorphosis or involution to colloid or resting state. He classified the adenomata into three groups, according to the amount of differentiation, namely simple (or colloid) adenoma, intermediate adenoma and fœtal adenoma, and all three groups may be met with at any phase of the cycle. It is interesting to note that Marine examined 617 pathological thyreoid glands or portions removed at operation or autopsy; 141 consisted of or contained benign epithelial tumours, but only 93 were sufficiently free from complications or destructive changes to be used for his study. He would like to regard these benign epithelial tumours of the thyreoid as "partial tumours," tumours that are funtionally only partially independent structures, as is shown by their reaction to iodine.

The definition, description and classification of adenomata in most works of reference are not very lucid. Ewing,[3] for example, divides epithelial overgrowths in the thyreoid into (i) simple goître, (ii) Graves's disease and (iii) true tumours and he reveals his suspicions of the adenomata by placing them with simple goître as benign tumours or tumour-like processes, whereas his true tumours are carcinomata. We hold that this attitude is unduly conservative. Many adenomata have at least as much right to the term tumour as, for example, fibro-myomata of the uterus. Ewing holds that: "the correct interpretation of hyperplastic processes in the thyreoid demands special standards dependent upon the development, structure and functions of this gland and not applicable elsewhere." Whilst we must admit that every glandular organ has special features in its development and function which have a special bearing upon its tumours, yet we feel that the special difficulty in thyreoid pathology lies in the fact that we are ignorant not only of the cause of neoplasms, but also of the origin of the stimuli that lead to either physiological or pathological hyperplasia; the frequent association of both tumours and hyperplasias in the thyreoid gland appears to be generally accepted. There appears to be no more evidence of undifferentiated embryonic cell rests in the thyreoid gland than Nicholson[4] has been able to demonstrate in other organs. The groups of interalveolar cells are probably rightly regarded as normal, fully differentiated thyreoid cells and the origin of adenomata is unexplained by this theory. The simple adenomata are the most differentiated, have the greatest iodine content and react most readily to iodine treatment; the fœtal adenomata are the least differentiated and so on. Adenomata are very susceptible to destructive metamorphoses (degenerations). Hæmorrhage is the most common. The degenerations occur usually in the oldest, that is the central part of the tumours. Œdema, usually due to venous and lymphatic stasis, is often encountered. It may go on to myxomatous changes. Fibrosis and atrophy due to circulatory defects come next. Hyaline degeneration and calcification must also be mentioned. The adenomata of the thyreoid, like fibroids of the uterus, are very rarely seen in animals (Marine, Aschoff[5]) although hyperplasia is common. It is singular that the adenomata should be so common in human goître and almost absent in the domestic animals. This is Marine's chief objection to his own hypothesis, namely, that the stimulus to benign tumour growth is the stimulus that excites the thyreoid as a whole to overgrowth. Marine originally held that the adenomata develope only up to puberty, though they might thereafter persist throughout life, but later he states that they may rarely develope later than adolescence.

Contemporary German opinion definitely accepts the encapsulated nodules as true tumours, adenomata (von Gierke,[6] Aschoff). For example, Aschoff writes: "We were able to show that the nodular form was not a kind of hyperplasia or hyperplastic condition, as was then believed, but that we were dealing with a definite tumour condition, namely, adenomata." Whilst rejecting Wölfler's theory of an origin from fœtal thyreoid rests and stating his opinion that they originate in normal thyreoid tissue, he goes on to qualify this somewhat by saying that the tissue of origin is usually the central follicles of lobules, follicles which he could distinguish by their elongated, even branching form and somewhat higher and deeper staining epithelium and he suggests that these follicles represent a germ layer of minute follicles of the thyreoid lobules. He has observed minute adenomata as darkly stained epithelial follicles lying close together, without colloid and without a capsule. Their increase in size causes compression and atrophy of the adjacent thyreoid tissue and a capsule is formed when they approximate the size of a cherry stone. Aschoff emphasizes one point

which we too have found very useful, namely, that in adenomata the lobular structure of the normal gland is not found. There is not a regular subdivision into lobules owing to the unicentric growth of these tumours. Also whilst colloid is only exceptionally seen in the lymph spaces of normal tissue, it is frequently found between follicles in colloid-containing adenomata. Aschoff found, too, that adenomata are as common in goître-free as in goîtrous populations, but in the former they are of microscopical size. The increased size in the latter is said to be due to the increased functional activity of the thyreoid in the goîtrous peoples.

Before passing to the histological details of some typical Sydney cases we wish to stress certain characters which we have frequently found.

(i) The presence of a capsule which makes it possible to shell out the tumour, sometimes with ease; surgeons appear to avail themselves of this peculiarity. A number of our specimens were shelled out at operation without removing appreciable non-tumour tissue. (ii) The absence of lobular structure already referred to. (iii) The peculiar blood vessels. In the normal gland these run in the inter-lobular septa and only a capillary network is found in the gland units (Williamson and Pearse.[7]) In most of our thyreoid material the smaller vessels appear to be empty of blood, but in many of the adenomata there are numerous irregularly placed, widely open blood sinuses with only an endothelial lining and they frequently contain blood corpuscles. (iv) The stroma is often more abundant so that the follicles appear to be spaced out and the stroma is often a hyaline-looking though weakly eosinophile ground substance. Into this tissue and into the follicles hæmorrhages are common and appear to lead mostly to central degenerations and so called cyst formations. (v) The structure varies much in different parts of the same adenoma.

We shall not discuss in this place the structure of the non-tumour thyreoid in adenomata nor the subject of the toxic adenomata or hyper-functioning adenomatous goître.

Case Reports.

Case I (reference number D425).—L.G., female, married, *ætatis* thirty-seven years at operation had a palpable tumour the size of a hen's egg in the mid-line, firm and painless. There were no toxic symptoms. At operation the tumour which was said to be covered by thyreoid tissue, was shelled out of the isthmus. The histology of portion of a section is shown in Figure II. It is encapsulated by fibrous tissue and consists of alveoli of varying size and shape and small clusters of cells without lumina. The larger alveoli are in a minority and have often a flattened epithelium and contain colloid. The smaller alveoli have a more cubical epithelium and usually do not contain colloid. Some alveoli are really short tubules. The groups of interalveolar cells are closely packed in places to form a more solid cellular tissue. The blood vessels are characteristically thin walled, usually only an endothelial lining, and groups of thyreoid cells are closely associated with the thin walls of some large sinusoidal vessels. The connective tissue has the common structureless character of adenomata. In one or two places there is a tendency to form cystic spaces with papillæ. The tumour was classified as an adenoma.

Case II (reference number F227, also *post mortem* number 4,277).—L.V., female, married, *ætatis* thirty-seven years at operation, had a slight enlargement of the neck for six years. She became pregnant five months before operation and had X ray treatment four months before. Her pulse rate was 100; there were exophthalmos and tremor and her basal metabolic rate was +10%. She was given Lugol's iodine 0·18 cubic centimetres (three minims) three times a day for a week and then a tumour was removed from the thyreoid. It was not covered by other thyreoid tissue. Microscopically it was seen to be an adenoma consisting of small and minute alveoli, some containing colloid, and the stroma revealed so-called hyaline degeneration. Whole areas were quite necrotic due to hæmorrhage. The vessels were thin walled. The patient was discharged cured. Seven months later she had a hysterectomy and died from an abscess of the broad ligament and pyæmia. At the *post mortem* examination the remainder of thyreoid weighed forty-five grammes (see Figure III).

Case III (reference number B255, Museum number 312.—S.I., female, single *ætatis* twenty-one years at operation, had an enlargement of the neck for ten years, increasing during the last twelve months. She had some dyspnœa and dysphagia, but no toxic symptoms. The tumour was about the size of a hen's egg in mid-line merging into the lateral lobes. At operation the tumour was readily removed. Several pedicles were ligated. It was an ovoid tumour approximately six by four centimetres. The cut surface showed coarse lobulation and a central hæmorrhagic area. Microscopically it was found to consist of small tubules and groups of minute alveoli separated by characteristic connective tissue from similar groups, resembling fœtal structure. There were thin walled blood vessels and in places stroma was degenerate. The lumina of the tubules and alveoli were too small to show colloid. This adenomatous tissue appeared to be spreading into thyreoid tissue consisting of large colloid alveoli, but there was no other evidence of malignancy and the tumour was classified as an adenoma. The patient was discharged well (see Figures IV and V).

Case IV (reference number B128, Museum number 315).—S.Y., female, married, *ætatis* twenty-seven years at operation, had an enlarged thyreoid (right side) for seven years, increasing during the last six months. It was a swelling the size of a small orange, movable, with a cystic feeling, not painful and not causing pressure symptoms. There were no toxic symptoms. It was shelled out with ease and was found to be an adenoma of spherical form, five centimetres in diameter, dark brown on section and with a definite capsule. Microscopically it was seen to consist of closely packed thyreoid alveoli of minute and small size and numerous groups of cells without lumina; there were numerous hæmorrhages. The vessels had an endothelial lining around which was a so-called hyaline structureless stroma. It was classified as an adenoma (see Figures VI and VII).

Case V (reference number F324)—V.T., female, married, *ætatis* thirty years at operation, noticed a thyreoid enlargement at the age of nineteen and an operation was performed at twenty-two years. At twenty-seven years it enlarged again. There were no toxic symptoms. At operation a lump was shelled out of the right lobe. The cut surface of this tissue was pale, but there were dark areas of hæmorrhage and a large cystic space into which thyreoid tissue projected. Microscopical examination revealed an adenoma in which were numerous hæmorrhages and areas of degeneration. It possessed a fœtal type of structure but numerous colloid containing alveoli. The vessels had only an endothelial wall. Trabeculæ were absent. It was classified as an adenoma (see Figure VIII).

Case VI (section from the Sydney Hospital through Dr. Keith Inglis).—M.S., female, *ætatis* thirty-eight years, had an enlargement of the thyreoid for twelve months. She had hoarseness and a choking feeling for three months. An area of enlargement was removed but the surgeon did not note any tumour. At the Pathological Department a tumour with a central hæmorrhage was found. No cysts or colloid were seen in the interior.

Microscopical examination revealed a predominance of tubule and column formation and these were very elongated in places. There were relatively few alveoli, minute, small and medium. Colloid was sparsely present in the tubules, more often in the alveoli. The epithelial cells were cubical or high cubical. The connective tissue was not abundant, but was characteristic and the blood vessels had only an endothelial lining as a rule.

(To be continued.)

APPENDIX TO Dr. OLIVER LATHAM'S ARTICLE ON "SOME OBSERVATIONS ON THE EXAMINATION OF THE CEREBRO-SPINAL FLUID"

(see page 336).

TABLE II.—CLINICAL STATES, THE TESTS USED AND THE REACTIONS COMMONLY FOUND IN THE CEREBRO-SPINAL FLUID.

Clinical Condition.	Pressure.	Foam.	Colour.		Glucose.	Pellicle.	Specific Germs.	Cells.		Protein.		Precipitate with—		Bordet-Wassermann Test.		Goldsol or other Colloid.	NaCl.
			Plain Blood.	Yellow, with or without Blood.				Lymphocytes and Mononuclear Cells.	Polymorphonuclear Cells.	Globulin.	Albumin.	$HgCl_2$ 1%	Salicylic Acid.	With Blood.	With Cerebro-Spinal Fluid.		
Sunstroke, meningismus and allied conditions, i.e., lead	+++	?	—	—	N	?	N	N	N	N or ?	N or ?	N or ?	N or ?	N	N	N	N
"606" poisoning	+++	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Intracranial or spinal hæmorrhage	+++	+	?	+++	N	—	N	N	N	+	+	+	+	N	N	N or ?	N
Obscure inflammations	+ or +++	+	N	N	N or D	+	N	?	?	?	?	?	?	N	N	?	N
Septic meningitis, diplo- or pneumococcal	+	+	?	?	D	+++	+++	N	+++	+	+++	+	+++	N	N	IV	N
Tabes or cerebral syphilis	+	+	N	N	N	?	?	+	N?	+++	+	+++	+	+++	+++	II or III	N
General paralysis of the insane	+++	+++	N	N	N	+?	?	+	+?	+++	+	+++	+	+++	+++	I	
Tuberculous meningitis	+	+	N	N	?	+	+	+	?	+	+	+++	+	N	N	N?	D
Encephalitis lethargica, poliomyelitis	+ or +++	+	N?	N	N or +	?	N	+	N	+?	+?	?	?	N	N	?	N
Epilepsy	+++	?	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Diabetes	N	?	N	N	+++	N	N	N	N	N	N	N	N	N	N	N	N
Uræmia	+++	+	N	N	N	N	N	N	N	?	?	?	?	N	N	N	N? or +
Drugs: Alcohol, ether, chlorofrom	+?	—	—	—	—	—	N	N	N	?	?	?	?	N	N	N	N

N = Normal or not present. + = Slight increase. +++ = Great increase. D = Diminished. ? = Not constant. — = Not known or unimportant. Cl = Cloudiness.

Intracranial or spinal hæmorrhage may be due to *encephalitis lethargica*. In Froin's syndrome there may be an excess of albumin and yellow colour only. A goldsol reaction may be obtained in disseminated sclerosis. In septic meningitis the sugar may be completely absent owing to the fermentative action of bacteria. In tabes curve II is the commonest. If pure blood is present, it is probably due to damage to a vessel by the needle. In general paralysis of the insane the polymorphonuclear leucocytes are increased after a congestive attack. In tuberculous meningitis the salt content is usually below 0·6% or 0·5%. There may be turbidity with sodium hydrate. In *encephalitis lethargica* the polymorphonuclear leucocytes are sometimes increased during the first few days and excess of urine is common. In several cases of apoplexy acetone may be present, but ammonia is not constant. In diabetes acetone at times is present. In uræmia the urea content is increased. This should be tested for. The chlorides are often much in excess. The permeability of the choroid varies in health and disease. The fluorescein test should be used.

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